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CLINICAL SIGNIFICANCE OF HEMOPTYSIS

Herman J. Moersch, M.D., Rochester, Minn.

The expectoration of blood is always an alarming experience for the patient and a matter of grave concern to the attending physician, because it may be the warning of serious disease. There is probably no symptom other than severe and acute pain that will stimulate a patient to seek medical aid as promptly as loss of blood for the first time from an unexplained source. When such bleeding occurs from the respiratory tract, the possibility of its being due to pulmonary tuberculosis or carcinoma of the lung is promptly suggested. It is unfortunate, indeed, that the severity of the bleeding is no guide as to the presence or absence of these diseases. It is imperative, therefore, that the patient with a history of hemoptysis have the benefit of thorough investigation to determine the cause of the bleeding.

It is essential first to determine that the bleeding does not originate from the oral cavity or nasopharynx. One should take similar precautions to be certain that the bleeding does not come from the gastrointestinal tract. Rarely, one encounters a malingerer who, for reasons known best to himself, gives a history of hemoptysis. In this case, the differential diagnosis can be extremely difficult.

PRESENT STUDY

This report is based on a study that was made to determine the diagnostic significance of hemoptysis and the frequency with which it occurs in cases of pulmonary disease. In a period of slightly less than six months, Jan. 1 to June 10, 1950, inclusive, bronchoscopy was performed in 670 cases at the Mayo Clinic. A history of hemoptysis was obtained in 200 (29.8%) of these cases. In 1947, Abbott and Hopkins [1] reported that a history of hemoptysis was obtained in 421 (31.9%) of 1,316 cases in which the patients came under the observation of a thoracic surgeon.

Table 1 shows the causes of the hemoptysis in the 200 cases that form the basis of this report. This table does not necessarily furnish any indication of the cause of hemoptysis among the population as a whole. The present group of cases in many ways is selective, because bronchoscopy is not performed in many cases in which active pulmonary tuberculosis, pneumonia, mitral stenosis, and other types of heart disease produce hemoptysis. In spite of such shortcomings, the present study does afford a good index as to the importance of hemoptysis as a clinical symptom.

Of the 200 patients, 123 were men and 77 were women. The ages of the patients ranged from 16 to 74 years, the average age being 48 years. The average age of the patients with bronchogenic carcinoma was considerably greater than that of the patients with bronchiectasis. That one cannot place too much reliance on age alone in arriving at a diagnosis is evident from the fact that the average age of the patients with chronic bronchitis and of those with hemoptysis of indeterminate origin was the same as that of the patients with bronchogenic carcinoma. Hemoptysis occurred most frequently in the patients between 50 and 59 years of age. In the decades above and below this one, the incidence decreased progressively.

Malignant tumors of the bronchus, trachea, or lung were the most frequent causes of the hemoptysis. A malignant tumor of one of these structures was present in 59 (29.5%) of the 200 cases in which there was a history of hemoptysis. Bronchogenic carcinoma was the most frequent type of malignant lesion encountered in the 200 cases (table 2). Bronchogenic carcinoma was present in 91 of the entire group of 670 cases in which bronchoscopy was performed. It is interesting to note that hemoptysis occurred in 48 of the 91 cases of bronchogenic carcinoma.

In cases of bronchogenic carcinoma, hemoptysis tends to occur more frequently when the lesion arises in the main stem bronchus than when it arises in the peripheral

From the Division of Medicine, Mayo Clinic.
Read before the Section on Diseases of the Chest at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

1. Abbott, O. A., and Hopkins, W. A.: Clinical Significance of Hemoptysis: A Study of 1316 Patients with Chest Disease, J. M. A. Georgia **36**: 360-371 (Sept.) 1947.

portion of the lung. Although the bleeding is frequently of recent origin in such cases, its duration is not always significant in the differential diagnosis, as is illustrated by the following case.

CASE 1.—A 58-year-old man had been well until six years before he came to the clinic. He had begun to expectorate blood and had continued to do so daily for three months. Roentgenologic examination of the thorax had not disclosed any abnormality, and the bleeding had been thought to be due to the excessive use of tobacco. During the next five and a half years, he had had intermittent episodes of hemoptysis. During the three months before he came to the clinic, he had expectorated blood daily and had been aware of a gradually increasing stridor.

When the patient was observed at the clinic he was expectorating blood. Physical examination disclosed an inspiratory stridor, which was best heard when the patient was in the recumbent position. Roentgenologic examination of the thorax revealed rather pronounced localized thickening of the apex of the right lung and an adjacent intrapulmonary nodule (fig. 1). There was a triangular shadow of density in the right cardiophrenic angle. Cytological examination of the sputum revealed carcinoma cells. Bronchoscopy disclosed a tumor arising from the right bronchus at the level of the lower lobe, and biopsy revealed that the tumor was an adenocarcinoma grade 4.

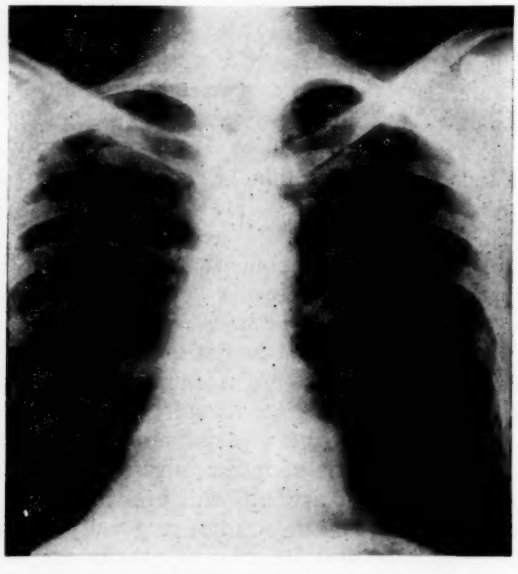

Fig. 1 (Case 1).—Bronchogenic carcinoma of the right lung.

In contrast with cases of bronchogenic carcinoma, in which bleeding usually has occurred for a relatively short time, in cases of adenoma of the bronchus the bleeding may occur for a much longer time. It has also been my experience that the bleeding in cases of adenoma of the bronchus may be more copious than in cases of bronchogenic carcinoma and that it is more often associated with evidence of suppurative infection. Adenoma of the bronchus occurs in a somewhat younger group of patients than carcinoma of the lung.

A metastatic tumor of the lung occasionally causes hemoptysis, as it did in three of the 200 cases. In fact, it may produce a clinical picture identical with that of bronchogenic carcinoma if the metastatic tumor involves a bronchus, and the diagnosis must rest on microscopic examination of tissue removed from the lesion. A malignant tumor of the trachea was present in two cases. This is an abnormally high incidence for this lesion, which is relatively uncommon. Alveolar carcinoma of the lung was present in one case. Bronchiectasis was found to be the second most common cause of hemoptysis. It was present in 53 (26.5%) of the 200 cases in which there was a history of hemoptysis and in 97 of the 670 cases in which bronchoscopy was performed. The severity of the bleeding varied greatly. In one case, the bleeding was so resistant to treatment that the involved lobe of the lung was removed in order to control it. In the cases of bronchiectasis in which hemoptysis occurred, it invariably could be precipitated by overexertion, and it often was associated with acute infection of the respiratory system. The dry type of bronchiectasis especially can present an extremely difficult diagnostic problem, and in most cases a definite diagnosis cannot be made until bronchography has been performed.

TABLE 1.—*Causes of Hemoptysis in 200 Cases*

Cause	No. of Cases
Malignant tumors	59
Bronchiectasis	53
Chronic bronchitis	18
Pulmonary tuberculosis	11
Pulmonary abscess	10
Middle lobe syndrome	6
Pneumonitis	6*
Broncholithiasis	4
Indeterminate	15
Postoperative atelectasis	2
Bronchial stenosis	2
Foreign body in bronchus	2
Emphysema	1
Boeck's sarcoid	1
Pulmonary infarction	1
Bronchogenic cyst	1
Neurofibroma of thoracic wall	1
Thyroiditis	1
Injury of thorax	1
Amebic abscess of liver and bronchopleural fistula	1
Mitral stenosis	1
Mediastinal teratoma	1
Chronic granuloma of lung	1
Fibroma of bronchus	1
Total	200

* In one case the pneumonitis was due to oil.

TABLE 2.—*Classification of Malignant Tumors*

Type of Tumor	No. of Cases
Bronchogenic carcinoma	48
Metastatic carcinoma of lung	3
Adenoma of bronchus	3
Cylindroma of trachea	2
Carcinoma of trachea	1
Alveolar carcinoma of lung	1
Lymphosarcoma of lung	1
Total	59

In the 53 cases in which bronchiectasis was associated with hemoptysis, the average age of the patients was 40 years; in the 44 cases of bronchiectasis in which there was no history of hemoptysis, the average age of the patients was 24 years. This apparent difference in the average age of the patients in these two groups of cases is chiefly attributable to the duration of the disease. Hemoptysis is prone to occur in cases of pulmonary abscess. In such cases, the bleeding usually is profuse.

Tuberculosis was found to be a less frequent cause of hemoptysis than it generally has been said to be by most authors. This difference can in some measure be explained by the fact previously mentioned, namely, that this study was based on a rather select group of patients, and by the fact that many patients who have active pul-

monary tuberculosis associated with hemoptysis would not be referred for bronchoscopic examination. By the same token, figures on the relative frequency of hemoptysis in cases of tuberculosis and in cases of other diseases, obtained by studies of patients in tuberculosis sanatoriums, would be in error in the opposite direction. It

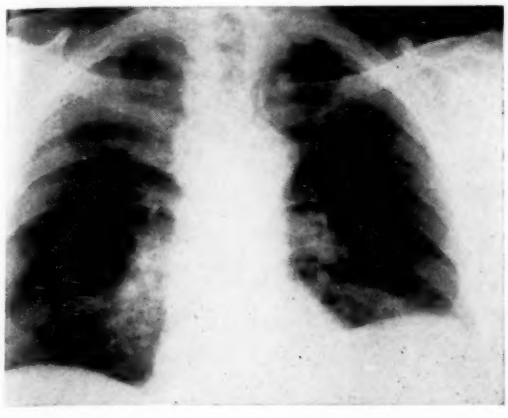

Fig. 2 (Case 2).—Elevation of the left half of the diaphragm.

is generally agreed that bleeding occurs less frequently in tuberculosis than in carcinoma of the lung. The possibility of tuberculosis must always be seriously entertained in any case of hemoptysis of unexplained origin.

Cardiovascular disturbances, such as mitral stenosis, pulmonary infarction, pulmonary hypertension, and aortic aneurysm, may give rise to hemoptysis, which may often present an extremely difficult diagnostic problem. It is needless to point out that the line of investigation that is to be employed in a case of hemoptysis must of necessity vary with the severity of the bleeding, the patient's general condition and age, and the various social and economic problems that are ever present. Unfortunately, the severity of the patient's hemoptysis is no index to the seriousness of the underlying disease.

A carefully taken history can often be an excellent guide as to the source of the bleeding and its underlying cause. It is surprising how accurate a patient can be in localizing the source of the bleeding. A history of expectoration of calcareous material or of the aspiration of a foreign body can well lead to the establishment of the correct diagnosis.

Case 2.—A 64-year-old man came to the clinic because of expectoration of blood, coughing, and a previous diagnosis of unresolved pneumonia. He had been perfectly well until seven months previously, at which time he had aspirated a piece of beef bone into his lung. He had coughed violently for 24 hours, and the coughing had then become less severe. Soon after this, the cough became productive of purulent material; it was worse in the morning and on retiring at night. Five months before the patient came to the clinic, a diagnosis of pneumonia had been made by roentgenographic examination of the thorax. He had been placed in a hospital. Antibiotics had produced improvement, but he had still continued to cough. A diagnosis of unresolved pneumonia and bronchiectasis had been made. About three months before the patient came to the clinic, he had started to expectorate blood. The hemoptysis had continued until he came to the clinic.

Physical examination of the thorax revealed increased dulness posteriorly at the base of the left lung and suppression of breath sounds in this area. Roentgenographic examination of the thorax revealed elevation of the left half of the diaphragm (fig. 2). Microscopic examination of the sputum did not disclose any acid-fast micro-organisms, and cytological examination of the sputum did not reveal any malignant cells. Bronchoscopic examination revealed a large piece of beef bone obstructing the right main stem bronchus at the level of the middle lobe. This was easily removed, and the patient's symptoms promptly subsided.

It is of interest to note that the patient localized the source of bleeding to the right side of the thorax, although he had been told that his difficulty was confined to the left side.

A careful physical examination of the thorax, a procedure that all too frequently is neglected, can be most rewarding in the study of hemoptysis. The character of respiration, the presence of stridor, the odor of the breath, and the contour and movement of the thoracic wall may furnish useful information. Clubbing of the fingers and the character of the sputum, especially after inversion of the patient, make the diagnosis of bronchiectasis a relatively easy one. A careful search should always be made for enlarged lymph nodes, particularly in the supraclavicular fossa; if such nodes are found, one should be removed for diagnosis. Although the microscopic examination of such a node usually reflects the character of the intrapulmonary disease causing the bleeding, this is not invariably so, as is illustrated by case 3.

Case 3.—A 62-year-old man first came to the clinic in 1947, because of a disease of the skin. A roentgenogram of the thorax made at that time revealed calcified lymph nodes in the hilum. Cultures of the sputum and gastric washings did not disclose Mycobacterium tuberculosis. In the next three years, the patient had recurrent attacks of hemoptysis but otherwise felt well. Because of the bleeding, he returned for reexamination. At that time, a roentgenogram of the thorax disclosed an infiltrating lesion in the apical segment of the upper lobe of the right lung

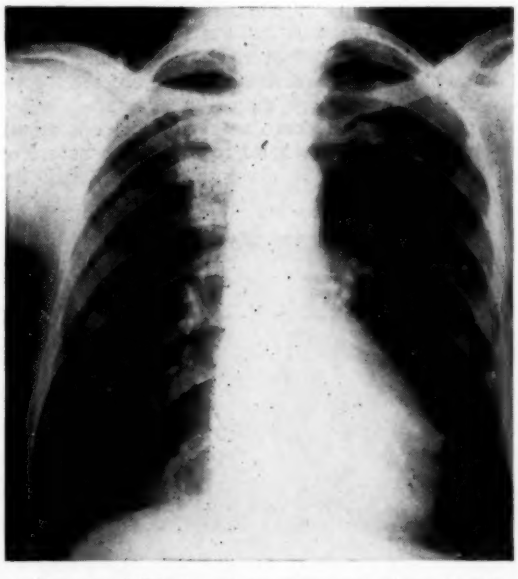

Fig. 3 (Case 3).—Infiltration of the upper lobe of the right lung in a patient with carcinoma of the lung.

(fig. 3). Microscopic examination of smears of the sputum did not reveal any tubercle bacilli, and cytological examination of the sputum did not disclose any carcinoma cells. The results of bronchoscopy were essentially normal, and examination of bronchial smears and washings did not disclose the presence of carcinoma cells or tubercle bacilli.

Palpation of the right supraclavicular fossa revealed a firm lymph node, which was removed surgically. Microscopic exami-

nation of the excised lymph node revealed a granuloma that was undergoing necrosis. Material obtained from the lymph node was used to make bacterial cultures and to inoculate guinea pigs. Both of these diagnostic procedures indicated that the lymph node contained tubercle bacilli. The clinical diagnosis was pulmonary tuberculosis. The patient died a short time after the diagnosis was made. Necropsy disclosed that the pulmonary lesion was a bronchogenic carcinoma.

Roentgenologic examination of the thorax is one of the most valuable aids in the study of patients with hemoptysis and should be used routinely in all cases of this type. It may enable one to determine not only the nature of the lesion but also its site and often its operability. Great care, however, must be exercised in those cases of hemoptysis in which the roentgenogram is noninformative, for a normal roentgenogram of the thorax does not rule out the presence of a pathological lesion.

In a case of hemoptysis in which roentgenographic examination of the thorax discloses a circumscribed lesion, but other routine tests fail to establish the diagnosis, it is often difficult to decide how to proceed. This is illustrated by case 4.

CASE 4.—A 40-year-old man had been well until two days before he came to the clinic, when he suddenly had expectorated a pint of bright red blood. He had felt well otherwise and had not had any fever. General physical examination did not disclose any abnormality. The urine was normal, and both the erythrocyte and leukocyte counts were within normal limits. Examination of the sputum did not disclose any tubercle bacilli or malignant cells. Roentgenographic examination of the thorax disclosed an area of infiltration in the upper lobe of the right lung (fig. 4).

In the course of bronchoscopic examination, a small amount of blood was seen coming from the upper lobe of the right lung. Examination of smears and washings obtained from the bronchus of the right upper lobe did not disclose the presence of any tubercle bacilli or malignant cells. The sputum and bronchial washings were used to make cultures for tubercle bacilli and fungi. It then became necessary to decide whether to perform an exploratory operation immediately or to observe the patient clinically until the reports on the cultures were available. The patient was reluctant to undergo an exploratory operation until we had obtained further evidence regarding the nature of the lesion. The thoracic lesion disappeared completely in five weeks (fig. 4*b*).

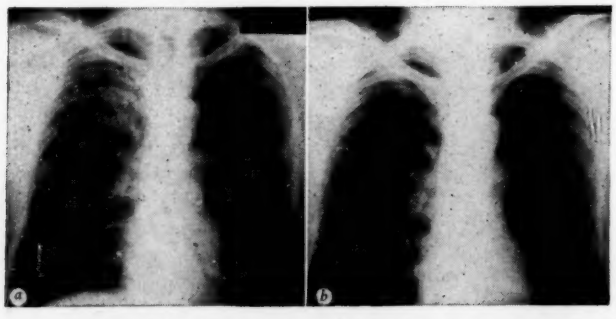

Fig. 4 (Case 4).—Infiltration of the upper lobe of the right lung (*a*) and disappearance of infiltration in five weeks (*b*).

The question always arises as to the best procedure to follow in any case of a solitary lesion of the lung with or without hemoptysis. Should such lesion be promptly explored, or should one wait for at least six weeks for the results of cultures and guinea pig inoculation, which should always be done with bronchial washings in cases of this type? Although no definite rule can be laid down, it would seem that, if the lesion has been known to be present for a considerable period of time, or roentgenographic examination shows evidence of calcification, one can well afford to observe the patient and await the results of these tests. In cases in which such evidence is lacking, it probably is best to perform an exploratory operation promptly, because of the high incidence of carcinoma in cases of this type.

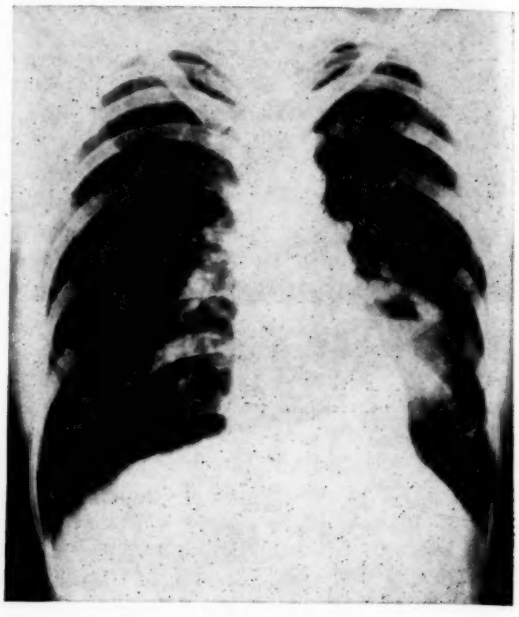

Fig. 5 (Case 5).—Abscess cavity in the lower lobe of the left lung in a patient with pulmonary tuberculosis.

Routine examinations of the sputum for tubercle bacilli should be carried out in every case in which there is a history of hemoptysis. It is not enough to examine the sputum directly for acid-fast organisms; the sputum should also be cultured. Culture of gastric washings for tubercle bacilli can often assist one materially in arriving at a correct diagnosis. It is not sufficient to examine the sputum and bronchial secretions for tubercle bacilli; they also should be examined cytologically for malignant cells. Although hemoptysis is rare in cases of fungous infection, this is a distinct possibility. Culture of sputum and bronchial secretions for fungi is always in order. Not only should culture for fungi be employed as a preoperative diagnostic procedure but it also should be used in the study of the surgical specimen, especially in cases of chronic granuloma or lesions of similar nature.

Bronchoscopy should be considered as a necessary diagnostic procedure in any case in which there is a history of unexplained hemoptysis. It often will reveal direct evidence of a lesion that will account for the bleeding, and it may enable the bronchoscopist to obtain a specimen of tissue or secretion directly from the lesion or site of involvement and thereby permit him to make a correct diagnosis, which otherwise might not be possible. This is illustrated by case 5.

CASE 5.—A 40-year-old woman had had a chronic cough for five years before she came to the clinic. The cough at times had been productive of mucopurulent sputum and masses of blood. The cough and expectoration had been aggravated by change of position. The patient's general condition was excellent; however, since she was at the clinic with her sister, she decided it might be a good idea to have a general examination.

Physical examination revealed increased dulness to percussion posteriorly at the base of the left lung and suppression of breath sounds over this area. Roentgenologic examination of the thorax revealed an abscess cavity in the lower lobe of the left lung (fig. 5), which contained fluid. Microscopic examination and cultures of the sputum did not reveal any tubercle bacilli. Cytological examination of the sputum did not disclose any malignant cells. On bronchoscopic examination, the posterior basilar division of the lower lobe of the left lung was found to be obstructed. Microscopic examination of a specimen removed from the site of obstruction revealed a chronic granuloma, which probably was due to tuberculosis. Cultures of secretions obtained directly from the site of obstruction produced tubercle bacilli. The lower lobe of the left lung was removed, and examination of the surgical specimen confirmed the diagnosis of tuberculosis.

In cases of hemoptysis of unexplained origin, it is often advisable to perform bronchoscopy while the bleeding is present, in order to trace the blood to its point of origin. Not infrequently, by this procedure one will detect a small lesion, which otherwise might not be detected.

Bronchography is a most useful procedure in cases of unexplained bleeding. It is by far the most valuable diagnostic method in the study of bronchiectasis. Its use should always be considered in any case of unexplained hemoptysis in a young person. It is best to postpone bronchography until the bleeding has subsided, as blood left behind in the bronchial tree might easily convey a false impression of the true state of affairs.

In 15 of the 200 cases in which there was a history of hemoptysis, the cause of the bleeding was classified as indeterminate (table 1). In four of the 15 cases, definite lesions were present in the lung. The patients in these cases were advised to undergo an operation, but they refused to do so because the exact nature of the lesion could not be established preoperatively. I feel that a malignant lesion probably was present in two of these four cases. In the 11 remaining cases, roentgenographic examination of the thorax did not disclose any evidence of a pulmonary lesion. In 7 of the 15 cases, bronchography was not performed for various reasons. Consequently, the presence of bronchiectasis could not be excluded definitely in these cases. In the remaining cases, various diagnostic procedures failed to disclose any cause for the hemoptysis. Although sufficient time has not elapsed to permit one to make a definite statement regarding the prognosis in these cases, it seems reasonable to assume that a serious lesion will not develop.

SUMMARY

A history of hemoptysis was obtained in 200 (29.8%) of 670 cases in which bronchoscopy was performed. The two lesions that were encountered most frequently in the 200 cases were malignant tumors of the trachea, bronchus, or lung and bronchiectasis. A malignant tumor of the trachea, bronchus, or lung was present in 59 (29.5%) of the 200 cases. Whenever a patient more than 40 years of age gives a history of hemoptysis, the presence of a malignant tumor should be suspected.

Bronchiectasis was present in 53 (26.5%) of the 200 cases in which there was a history of hemoptysis and in 97 (14.5%) of the 670 cases in which bronchoscopy was performed. In the 53 cases in which bronchiectasis was associated with hemoptysis, the average age was higher than in the cases in which bronchiectasis occurred without hemoptysis. (This apparent difference in the average age in the two groups of cases is largely attributable to the duration of the disease.)

In 17 (7.5%) of the 200 cases, the cause of the hemoptysis could not be determined. In cases in which a thorough clinical investigation, including roentgenographic examination of the thorax, fails to disclose any cause for the hemoptysis, there is an excellent chance that a serious pulmonary lesion will not develop subsequently. In this group of 200 cases, the hemoptysis occurred most frequently in the sixth decade of life. One hundred twenty-three of the patients were men, and 77 were women. The severity of the bleeding gave no indication of the nature of the underlying lesion.

CARCINOMA ARISING IN ADENOMAS OF COLON AND RECTUM

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One of the more difficult problems facing proctologists, abdominal surgeons, and pathologists is the question of proper treatment for adenomas in which carcinomas have arisen that have not yet invaded the muscular bowel wall. The decision must be made as to whether it is safe to treat these lesions by local removal or whether a radical resection should be performed immediately. In this paper, we hope to settle this problem at least partially.

In 1948, Scarborough and Klein [1] reported a study of 458 patients with polypoid disease of the colon and rectum. In this series there were six pedunculate adenomas of the colon for which bowel resection had been performed and in which areas of invasive carcinoma were found. Although there was no invasion of the pedicle in any case, there were regional lymph node metastases in three of the operative specimens. This report raised the question as to whether radical surgery should be performed for all adenomas showing microscopic malignant change. Since it had been the impression at Memorial Center that local excision of pedunculate adenomas, even with malignant change, constituted safe and adequate treatment, the present study was undertaken.

From 1937 to 1949, inclusive, there have been 265 cases of large-intestinal adenomas at Memorial Center.

This investigation was aided by a grant from the estate of Florina Lasker.

From the Colon and Rectum Service and Pathology Laboratories of Memorial Center for Cancer and Allied Diseases.

Read before the Section on Gastro-Enterology and Proctology at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

1. Scarborough, R. A., and Klein, R. R.: Polypoid Lesions of the Colon and Rectum, Am. J. Surg. **76**: 723-727, 1948.

In all cases there was adequate material for reliable pathological study, and the patients received definitive treatment. In 39 of these cases, there were adenomas that showed definite carcinomatous change. These 39 cases comprise only clinically benign adenomas in which foci of carcinoma were found on pathological examination.

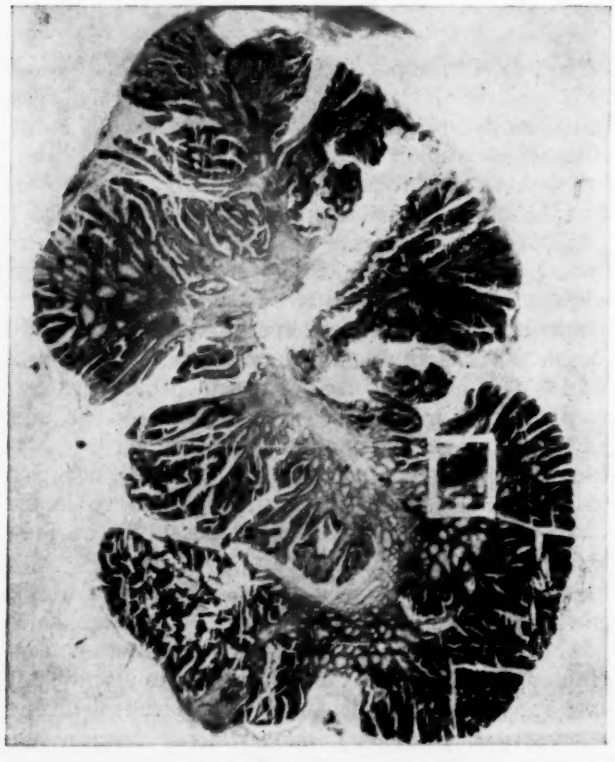

Fig. 1.—Pedunculate adenoma of sigmoid colon with in situ carcinoma. In the upper central portion the glandular elements have undergone carcinomatous change.

They do not include clinically apparent cancers that invaded the muscular bowel wall and in which remnants of benign adenomatous structure were found subsequently; also not included are papillary adenomas and adenomas showing only atypical epithelial hyperplasia.

INCIDENCE

Of the patients studied, 22 were men, and 17 were women, with approximately the same incidence in each sex of colonic and rectal cancer. The age incidence breakdown of malignant adenomas is as follows. There were 4 patients in the 31 to 40 year age group, 5 in the 41 to 50 group, 17 in the 51 to 60 group, 8 in the 61 to 70 group, and 5 in the 71 to 80 group. The youngest patient was 33 years old; the oldest was 76 years old; and the average age was 56.6 years. Of the entire series of 265 cases of adenomas, information on age was obtainable in 253. Of 164 patients in this series in whom the tumors of the large intestine were histologically benign adenomas, the average age was 51.6 years. Thus, the patients with adenomas showing malignant change were, on the average, five years older than those with benign lesions. Furthermore, the average age of the 39 patients is approximately the same as that of patients with fully developed colonic and rectal cancer. These figures are at variance with the average of 62.9 years for patients with papillary adenomas (villous tumors) previously reported by us [2]; however, because of the small number of cases under present consideration, undue significance must not be attributed to these variations. Information regarding family history of cancer was not available for 1 patient, and for 17, there was no cancer history. For the remaining 21 patients, there was a history of cancer in the immediate family; in 8 instances (and possibly in 2 others) the cancer had occurred in the gastrointestinal tract.

2. Sunderland, D. A., and Binkley, G. E.: Papillary Adenomas of the Large Intestine: A Clinical and Morphological Study of 48 Cases, Cancer 1: 184-207, 1948.

ANATOMIC DISTRIBUTION

In 20 cases, there was a single adenoma, and in 19 cases, multiple adenomas were found; however, in only 6 of the group of patients with multiple adenomas was malignant change found in more than a single adenoma. The anatomic distribution of adenomas showing carcinomatous change is as follows. In the 33 cases of cancer in only a single adenoma, the adenoma was situated in the rectum in 14 cases, in the sigmoid colon in 18 cases, and in the descending colon in 1 case. In the six cases in which the cancer appeared in multiple adenomas, the lesions

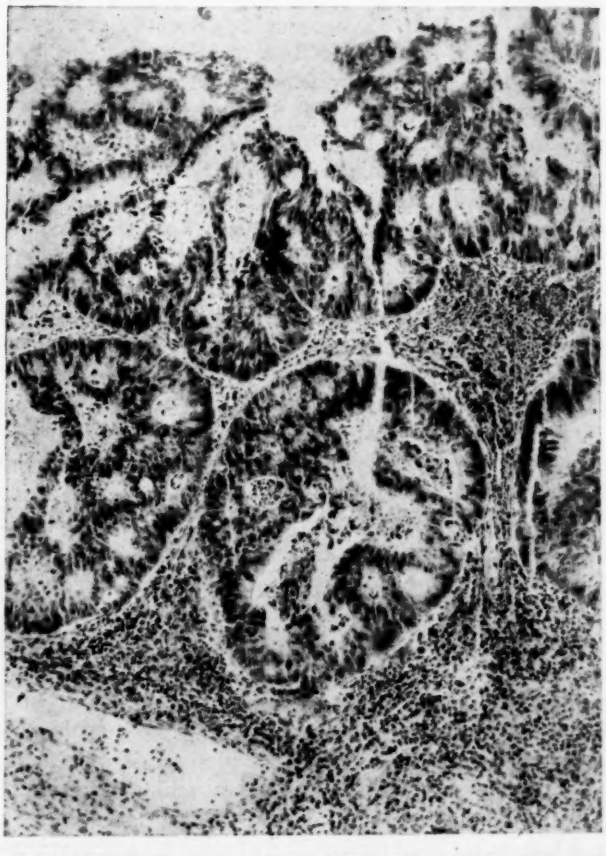

Fig. 2.—Higher power view of area indicated by rectangle in figure 1. Malignant transformation is obvious, but there is no demonstrable penetration of the basement membrane.

containing cancer were distributed as follows, one case each: sigmoid colon, sigmoid and transverse colon, rectum and descending colon, rectum and ascending colon, and sigmoid, descending, and transverse colon. In the 19 cases of multiple adenomas, the number of adenomas varied from 2 to more than 10 (8 cases); in some of the latter almost the entire colonic mucosa was involved.

PATHOLOGICAL CONSIDERATIONS

Many workers refuse to recognize a lesion as carcinoma until there is actual invasion through the muscularis mucosae; others, in direct contrast, regard adenomas as malignant whenever there is multiplicity of nuclear layers within the adenomatous glands; our viewpoint is

Fig. 3.—View of area indicated by lower right rectangle in figure 4, showing in situ adenocarcinoma.

intermediate. If one regards stratification of nuclei as an indication of malignant change, there would be few true adenomatous polyps that would escape the diagnosis of cancer; on the other hand, if invasion through the muscularis mucosae is considered a necessary criterion, one would be forced to the insecure position of maintaining that cancer is not malignant, in spite of typical malignant structure, until it actually begins to invade. In assuming this viewpoint, it is logical to deny the existence of in situ epidermoid carcinoma of the cervix, noninfiltrating epidermoid cancer of the bladder, and noninfiltrating duct cancer of the breast, all of which are generally recognized to be pathological entities. Therefore, we make a diagnosis of in situ carcinoma in an adenoma if the structure of some areas is identical with that seen in carcinoma actually invading the bowel wall, but, in the particular adenoma under consideration, there is no demonstrable penetration of the basement membrane. That our viewpoint is reasonable may be judged by figures 1, 2, and 3.

For the purpose of this study, we have divided the carcinomas occurring in these adenomas into in situ and invasive groups. The latter designation is reserved for those that have broken through the basement membrane and are invading the framework of the polyp, with or without complete penetration through the muscularis mucosae. If any doubt existed as to penetration of the basement membrane, the lesion was classified as in situ. Of the cancers studied, 23 were in situ, and 16 were definitely invasive. Five of the invasive carcinomas had penetrated the muscularis mucosae completely; five had invaded it partially; in the remaining six, the invasion of the framework of the polyp appeared to be superficial to the muscularis mucosae. Examples of invasive carcinomas are shown in figures 4 and 5.

In 24 cases, the adenomas were pedunculate; in 15 cases, they were not; all the adenomas had constricted bases and were movable. The diameter of the pedunculate adenomas varied from 0.4 to 8 cm.; whereas the diameter of the nonpedunculate adenomas varied from 1 to 7 cm. Of the 24 pedunculate lesions, 16 measured 2 cm. or less in diameter as compared to 8 of the 15 with flat attachment that measured 2 cm. or less. In 9 of these 39 cases, there was an independent invasive cancer of the large intestine, apart from that found in the adenoma. In only one of these cases was there definite microscopic evidence of residual benign adenoma in the independently occurring carcinoma.

TREATMENT AND RESULTS

Adenomas of the large bowel are best treated by complete removal. As we shall discuss later, local removal has resulted in cure, in our experience, although adenomas may be expected to develop in other locations in subsequent years.

Treatment of adenomas of the rectum is a comparatively simple procedure, since these lesions are accessible to inspection and local removal. They may be removed by fulguration en masse, local excision with scalpel and suture of mucosa, clamping and ligation of base

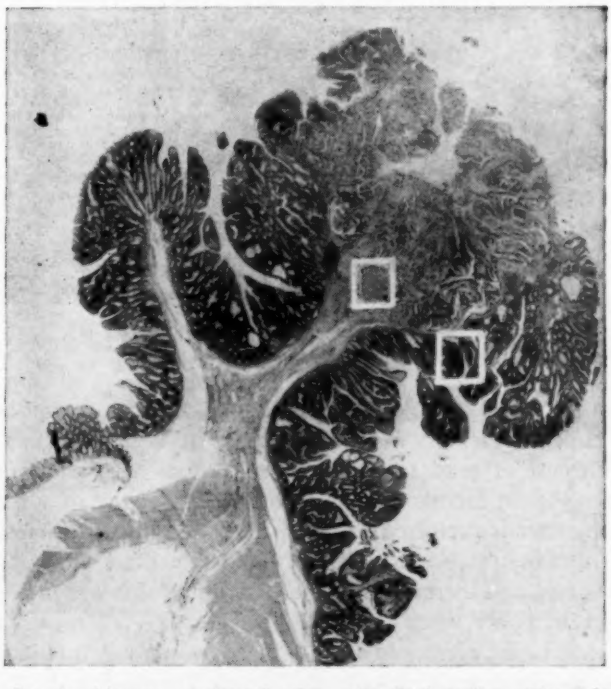

Fig. 4.—Adenoma of sigmoid colon, with distal portion replaced by infiltrating carcinoma. Although not pedunculate, the lesion is projecting; it was removed by segmental resection, and the regional lymph nodes contained no metastases.

or pedicle before removal, and excision by means of the cautery snare. Fulguration or desiccation en masse, although not the best method of treatment, is employed extensively by others. The objectionable feature of this method is the destruction of cells, which prevents histological examination of the tumor; moreover, perforation,

with peritonitis, has occasionally followed this method. We employ fulguration only for the minute lesions that cannot be removed by any other means and for the occasional small tags remaining after snare removal. Local excision and suture produce good results. This method is difficult to carry out when the lesion is high in the rectum. Clamp and ligation is occasionally the method of choice for the broad pedicle of a large adenoma in the midsection and lower section of the rectum.

Our choice of routine method for removing adenomas of the rectum and lower sigmoid is the cautery snare. The technique of cautery snare removal of polyps has been described elsewhere and need not be repeated in detail. Experience has shown that scopes of different lengths and diameters are necessary. A large operating scope, 18 cm. long and 3 cm. in diameter, is useful for removing polyps

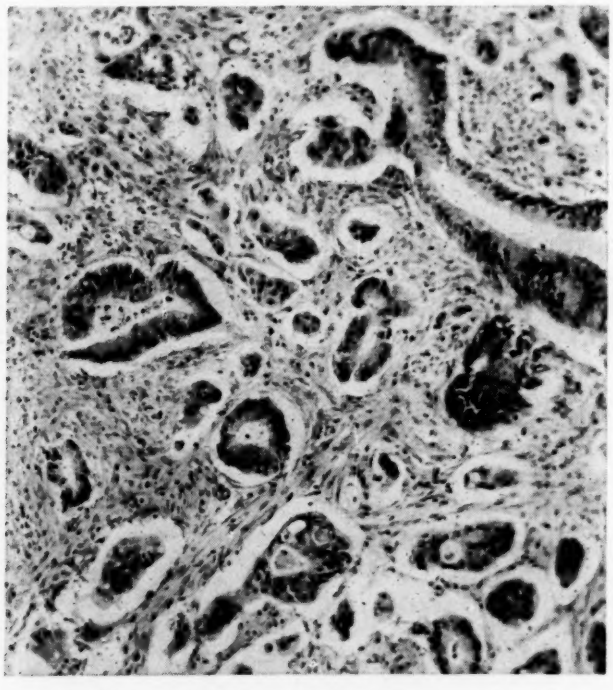

Fig. 5.—View of area indicated by upper left rectangle in figure 4, showing obviously invasive adenocarcinoma.

in the rectal ampulla, whereas a long, narrow sigmoidoscope is necessary for some of those in the lower colon. The use of caudal anesthesia and proper positioning of the patient facilitates the operation. Snare wire of small diameter is preferred for routine use. Small wire snares are easily placed about either the pedunculate or sessile lesions, and there is a minimal amount of damage to adjacent tissue when the wire is tightened. We prefer a coagulating current to prevent bleeding and rely on tightening the snare to cut through tissue. The pedicle should be severed close to the bowel wall, and, when dealing with the nonpedunculate variety, the wire should include all tissue about the polyp down to the circular muscle fibers of the wall. The most satisfactory removal excises a circular area of mucosa beyond the polyp and leaves the muscle fibers exposed.

3. Colvert, J. R., and Brown, C. H.: Rectal Polyps: Diagnosis, 5 Year Follow-Up, and Relation to Carcinoma of the Rectum, Am. J. M. Sc. 215: 24-32, 1948.

Treatment of adenomas of the colon is not difficult but necessitates laparotomy. Patients should be afforded appropriate preoperative preparation, the chief feature of which is a clean, empty bowel for inspection. This can be achieved by the administration of magnesium sulfate (epsom salt) in sufficient quantity to produce five to eight stools daily during a five day period and 2 oz. (56.70 gm.) of castor oil 20 hours before operation.

Adenomas previously found roentgenographically can usually be located by palpation. Routine colotomy, once the adenoma is located, consists of an incision, 4 to 5 cm. in length, through the longitudinal band near the polyp. The pedicle is ligated near the base and divided. The incision is closed with a continuous fine absorbable surgical (catgut) suture in the mucosa and a layer of interrupted silk sutures through serosa and muscularis.

Any operation for adenomas of the colon must include a careful examination of the colon with a sigmoidoscope for additional adenomas in the remainder of the colon. If found, these should be removed. Instrumental examination of the colon and snare removal of polyps is easily carried out when the bowel is free of fecal material. The operator will require, in addition to the usual laparotomy instruments, a sigmoidoscope 25 to 30 cm. in length and 2 cm. in diameter, the instruments necessary for cautery snare removal, and a long suction tube to keep the field clean. The entire colon can be inspected through two or three incisions into the bowel. When an associated invasive cancer is present, the treatment is the same as that for the primary carcinoma.

The results of treatment in the 39 cases under consideration are given in tables 1 and 2. Three patients were lost to follow-up one month to two years following removal of their adenomas. When last seen, they had had no recurrence. One patient, who had a subtotal colectomy for disseminated adenomatosis, is still alive four and one-half years after the operation but has residual adenomas in the rectal stump. Another patient, who had incomplete removal, had residual adenoma when last seen, but he subsequently had it removed by another surgeon. For 15 patients, more than three years have elapsed since their operation. All except the nine patients with independent cancers and the two patients with disseminated adenomatosis were treated only by some form of local removal.

SUMMARY AND CONCLUSIONS

The problem of treating of adenomas of the colon and rectum is rapidly increasing in importance because of the greater number being found today; this is the result of the growing realization of their potentially serious nature. Colvert and Brown [3] concluded that rectal polyps, when malignant, are usually of a low grade of malignancy. We disagree for two reasons. In the first place, among the 265 cases of this series, there were 10 independent cancers of large intestine (including the one in the group of 39 cases previously mentioned) in which definite microscopic evidence of residual benign adenoma was found. Two of these cancers were of the colloid type; the remainder were adenocarcinoma, grade 2. Four of the cancers had not penetrated the entire thickness of the bowel wall; three had invaded the adjacent mesentery; and three

had metastasized to regional lymph nodes at the time of removal. Three of the patients died of cancer less than three years after resection, and another patient had recurrent cancer six months postoperatively. In the second place, in a previous study made by us of the villous or papillary type of adenoma, it was found that in some of these cases cancers of the most malignant variety did occur [2] in the tumors.

In spite of the foregoing information, it is our opinion that cancer arising in a simple projecting adenoma that does not yet show lymphatic infiltration of the submucosa can safely be regarded as a local problem; however, we do believe that these are potentially malignant carcinomas, and, if they remain untreated, they will eventually invade, metastasize, and cause death. In our experience, no adenoma containing focal cancer has recurred or metastasized after local removal; however, our series is small, and the follow-up period for many patients is short. Thus, only tentative conclusions can be made.

The results of this investigation are comparable to those reported by McLanahan, Grove, and Kieffer [4] in their analysis of 38 cases of adenomas with malignant change that were confined to the rectum or lower sigmoid colon. All were removed by conservative local measures. The authors stressed the fact that most of these patients can be cured by complete local eradication of the adenoma. In their series, adenomas recurred in 10 cases, and in 5 of these the recurrent lesions were definitely carcinoma; however, in some of the original tumors, there had been actual invasion of the bowel wall, and no distinction was made between simple and papillary adenomas.

Our present knowledge, although incomplete, confirms our previous belief that cancer that has arisen in a simple adenoma and has not yet invaded the submucous lymphatics can be safely removed from the rectum by cautery snare and from other locations in the colon by simple colotomy and division and ligation of the pedicle or by snare removal, without fear of subsequent recurrence or metastasis. If at the time of laparotomy for a colonic adenoma there is any suspicion that invasive cancer is present in the base, a wide bowel resection and lymph node dissection should be done. Of course, any patient who has had an adenoma removed should be carefully followed with a view to detection of new adenomas.

TABLE 1.—*Results of Treatment of Patients Without Cancer Independent of Adenomas*

Site and Treatment Method	Living Without Disease Less Than 3 Yr	Living Without Disease 3-8 Yr.	Living with Disease	Died of Cancer	Lost to Follow-Up	Total
Rectum						
Cautery snare (complete)	3	3	0	0	2	8
Cautery snare (incomplete)	0	0	1	0	0	1
Surgical excision	1	0	0	0	0	1
Sigmoid						
Cautery snare (complete)	2	7	0	0	1	10
Colotomy and excision	3	0	0	0	0	3
Segmental excision	1	0	0	0	0	1
Rectum and Sigmoid						
Cautery snare plus colotomy and excision	1	1	0	0	0	2
Cautery snare alone	0	2	0	0	0	2
Disseminated Adenomatosis						
Colectomy	0	0	1	0	0	1
Polypectomy and colectomy	1	0	0	0	0	1
Total	12	13	2	0	3	30

TABLE 2.—*Results of Treatment of Patients With Cancers Independent of Adenomas**

Treatment (Various Sites)	Living Without Disease Less Than 3 Yr.	Living Without Disease 3 Yr. or More	Living with Disease	Died of Cancer	Lost to Follow-Up	Total
Abdominoperineal resection	3	2	0	1	0	6
Right colectomy †	0	0	0	1	0	1
Segmental resection †	0	0	1	0	0	1
No treatment of cancer †	0	0	1	0	0	1
Total	3	2	2	2	0	9

* Primary treatment was for independent cancer. † In addition, adenoma was removed by cautery snare.

121 E. 60th St. (Dr. Binkley).

4. McLanahan, S.; Grove, G. P., and Kieffer, R. F., Jr.: Conservative Surgical Management for Certain Rectal Adenomas Showing Malignant Change, J. A. M. A. **141**: 822-825 (Nov. 19) 1949.

Intraocular Foreign Bodies.—The removal of an intraocular foreign body is never a true emergency. A foreign object eventually becomes embedded in the ocular tissues, it is true, but the process does not occur immediately, and there is ample time for all necessary diagnostic measures and for bringing the patient to a properly equipped hospital and a properly qualified eye surgeon. Patients with intraocular foreign bodies are preferably transported recumbent, and always with both eyes covered. First aid measures . . . should be limited to simple cleaning of the external eye and the application of sterile bandages.—William B. Clark, The Management of Acute Ocular Injuries, *The Journal of the Medical Association of the State of Alabama*, January, 1952.

ATROPHIC PYELONEPHRITIS VERSUS CONGENITAL RENAL HYPOPLASIA

John L. Emmett, M.D., J. Jose Alvarez-Ierena, M.D.
and
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There has been much discussion in the urological and pathological literature regarding the unilateral, abnormally small kidney. Many confusing terms have arisen to describe it, such as atrophic kidney, contracted kidney, atrophic pyelonephritis, congenital hypoplasia, infantile kidney, aplastic kidney, and agenesia. Some statements in the literature tend to leave one with the impression that these various terms describe separate clinical and pathological entities that may be distinguished easily clinically, urographically, or by gross or microscopic examination. The two descriptive terms that have become most widely used are "chronic atrophic pyelonephritis" and "congenital hypoplasia." Contrary to general opinion, it has been our impression that it is usually difficult, if not impossible, to distinguish these two entities, if in reality two such separate entities actually exist.

A cursory review of the literature will reveal the great confusion that exists on this subject. Most standard American textbooks on urology base their classification and descriptions on an article written by Gutierrez [1] in 1933. In a review of the literature and a presentation of eight personal cases, Gutierrez attempted to make a classification of the congenitally small hypoplastic kidneys and to distinguish them from renal "atrophy" or "contraction" due to acquired causes. His classification suggested inclusion of three groups: (1) congenital hypoplasia, (2) renal aplasia, and (3) complete absence of a kidney (other term, complete agenesia).

Gutierrez' description of congenital hypoplasia states that the kidney is small and infantile in type but usually can be recognized grossly as a kidney. Excretory function is present (though usually diminished), and medullary and cortical substance is present. (Apparently on the basis of one case observed personally, he also suggested that there may be absence of pyramidal tissue. This subject will be discussed later.) There may be a rudimentary or hydronephrotic pelvis and calyces, which may be "bizarre" in size or position or even absent. The ureter is patent. Microscopic examination shows "normal or rudimentary glomeruli and tubules." Renal aplasia, on the other hand, shows no gross evidence of a true kidney, no pelvis, absence of a true renal pedicle, and an incompletely developed ureter that is not patent. There is no excretion of urine and no function. "Histologic section of the supposed renal mass reveals glomeruli and tubules showing arrest of development of the renal organ." As for the third group—congenital absence of one kidney (other term, complete agenesia)—Gutierrez stated that no kidney or ureter is present and no evidence of glomeruli or tubules microscopically. In nearly all cases the ipsilateral adrenal and the corresponding side of the vesical trigone are absent.

There is no doubt that this extensive and well-written article has done much to call attention of the profession to the hypoplastic or infantile kidney that cannot support life. The main thesis of the paper was to warn surgeons against removing a kidney unless they were sure that the opposite kidney was normal. There is one serious error in the paper, however: the lack of emphasis given to acquired causes of renal atrophy, such as obstruction and infection, which must be taken into consideration in differential diagnosis. That the possibility exists is apparent in Gutierrez' statement:

> It is very important, therefore, that the differential urographic diagnosis of the condition be borne in mind, since this abnormal type of kidney [congenital hypoplasia] may readily be confused with the presence or the association of other different types of lesions, such as are frequently observed in the acquired or secondary atrophy of one kidney, due to tuberculosis, tumor, calculous diseases, pyelonephritis or hydronephrosis.

Gutierrez also mentioned that the congenital hypoplastic kidney also can be the site of pyelonephritis, but he failed to mention how one can decide which is the primary cause of the "atrophy": infection and scarring, or congenital maldevelopment. As a matter of fact, of the two cases that he reported (which he observed personally) under the heading of congenital hypoplasia, one appears to be a case of definite hydronephrotic atrophy with pyelectasis and absence of renal pyramids. (This no doubt is the reason for his suggestion that "absence of renal pyramids" is found occasionally in congenital hypoplasia.) The condition in the other case, from the microscopic description, no doubt is one that anyone now would call "chronic atrophic pyelonephritis." The pathological description of this case is as follows:

> The specimen consisted of a kidney measuring 7 by 4 by 2.5 cm. The microscopic sections showed marked scarring of the cortex within large portions, disappearance of the glomeruli, dilatation or atrophy of the tubules, increased fibrous stroma and thickening of the arterioles with diminution of their lumina. The pelvic mucosa was heavily infiltrated by lymphocytes. The covering epithelium was not well preserved. In some of the thicker parts of the kidney more normal appearing glomeruli and tubules were seen, but even here there were streaks of scarring with varying stages of thickening of Bowman's capsule and fibrosis of glomeruli.

On the other hand, in 1922 Braasch [2] presented a study of 28 cases of unilateral, small kidneys removed surgically. Gross and microscopic examination left little question in his mind that the basic lesion was inflammation, with secondary fibrosis and contracture, although he admitted that in many cases there was minimal evidence of infection at the time of examination. He explained this on the basis of previous, "burned out" infection, rather than on the basis of congenital hypoplasia.

Read before the Section on Urology at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

From the Section of Urology (Dr. Emmett) and the Division of Surgical Pathology (Dr. McDonald), Mayo Clinic; Fellow in Urology, Mayo Foundation and University of Minnesota (Dr. Alvarez-Ierena).

1. Gutierrez, R.: Surgical Aspects of Renal Agenesis: With Special Reference to Hypoplastic Kidney, Renal Aplasia and Congenital Absence of One Kidney, Arch. Surg. **27**: 686-735 (Oct.) 1933.

2. Braasch, W. F.: Atrophic Pyelonephritis, J. Urol. **7**: 247-257 (April) 1922.

The experimental work of Goldblatt [3] greatly increased the interest of the profession in unilateral, small, "atrophic" or "contracted" kidneys. It also aroused considerable clinical discussion concerning the possibility of distinguishing congenital hypoplasia from acquired renal "atrophy" or "contraction."

German pathologists, such as Aschoff,[4] Haslinger,[5] Staemmler and Dopheide,[6] Fahr,[7] and Linder,[8] have written much on the subject of the "contracted kidney" found at necropsy. Their pathological observations include the bilateral contracted kidneys of nephrosclerosis and glomerulonephritis, as well as those that have become shrunken or contracted as a result of obstruction, stone, hydronephrosis, and infarcts. Haslinger [5] and Staemmler and Dopheide [6] recognized the pyelonephritic, contracted kidney as a definite clinical entity and did much to draw attention to the subject.

Linder [8] in 1937 made an excellent study of the "contracted kidney." He supported the hypothesis of infection and pyelonephritic contracture as the etiological factor in most "atrophic" or "contracted" kidneys. His hypothesis of pathogenesis mentions early changes of submucosal round cell infiltration in the tips of the papillae and surrounding calyceal fornices, followed by ascending pericanalicular infiltration and edema. Later there is absorption of this infiltration, resulting in peritubular fibrosis and constriction, which causes tubular dilatation (his so-called internal hydronephrosis) and, finally, glomerular hyalinization and atrophy. He further postulated that this fibrotic process could proceed until it produced a severe compressive disturbance of the arterial supply, resulting in ischemia and further renal atrophy.

Lieberthal [9] in 1939 tried to differentiate (by gross and microscopic examination) pyelonephrotic contracture, congenital hypoplasia, contracture secondary to nephrosclerosis, and contracture secondary to chronic glomerulonephritis. Among findings that to him suggested congenital hypoplasia were excessive reduction in size, scarcity or absence of glomeruli, decrease in number of pyramids, fetal lobulation, small blood vessels, and small pelvis and ureter. He pointed out that infection frequently was found associated with congenital hypoplasia. Findings that to him suggested pyelonephritic contracture were a normal number of papillae, many glomeruli, renal pelvis normal in size or larger, and the presence of lymph follicles in the interstitial tissue (evidence of previous intratubular infection—pyelonephritis). He further stated that contraction from nephrosclerosis should be recognized from the changes in the vessels, whereas the typical changes in the glomeruli should identify contracture from chronic glomerulonephritis. He stated:

> The demonstration of adhesions of the glomerular tuft to the peripheral leaf of Bowman's capsule and the presence of half-moon forms on the latter, will usually bear testimony to the previous existence of inflammatory changes in the glomeruli. But, in the advanced stages of contracture, the differentiation may be exceedingly difficult, and only the presence or absence of lymph follicles will tell us which condition we are dealing with.

Lieberthal did not mention the number of kidneys that he studied in order to arrive at his conclusions.

It is interesting to compare the statements of various authors regarding the urographic appearance of the pelvis, calyces, and ureter found in these various types of small kidneys. None of the statements made are in agreement, and the reader is left with the impression that probably there is no pyelographic deformity that is pathognomonic or helpful in the differentiation of the various types of "atrophy" or "contraction."

Since the emergence of the unilateral "atrophic" kidney as a factor of importance in occasional cases of hypertension, the subject has created renewed interest. In the hope that we might be able to contribute something to the clarification of this confused subject, this study was undertaken.

MATERIAL FOR STUDY

Selection of Cases.—It seemed reasonable that a study of a fairly large group of cases of unilateral "atrophic" kidney should supply a practical working answer to the general problem. To find such a substantial group of cases for analysis, we reviewed the histories of all patients in the Mayo Clinic files during the years 1935 to 1948, inclusive, for whom a diagnosis had been made that might indicate the presence of an abnormally small kidney. More than 5,000 histories were reviewed, with such diagnoses as pyelonephritis, chronic pyelonephritis, chronic atrophic pyelonephritis, contracted kidney, hypoplastic kidney, renal aplasia, deformed kidney, and renal atrophy. From this group we found almost 400 cases in which urograms indicated a definite reduction in size of the kidney.

In order to limit the study further, we excluded all cases in which the cause of the "atrophy" was apparent or in which associated pathological conditions existed. We thus eliminated cases of obstructive uropathy with associated pyelectasis, which, as is well known, leads to renal atrophy. Also eliminated from the study were cases with associated renal or ureteral calculi, cyst, and tumor. We also excluded patients with known "medical" diseases, such as glomerulonephritis and nephrosclerosis (usually bilateral, which would remove them automatically from this study).

Our prime motive in this undertaking was to determine whether unilateral hypoplastic or "atrophic" kidneys could be classified and differentiated. We were especially interested to see whether "atrophic pyelonephritis" was distinct from and could be differentiated from "congenital hypoplasia." Although the problem of the incidence

3. Goldblatt, H.: Studies on Experimental Hypertension: V. The Pathogenesis of Experimental Hypertension Due to Renal Ischemia, Ann. Int. Med. **11**: 69-103 (July) 1937; Experimental Hypertension Induced by Renal Ischemia, Bull. New York Acad. Med. **14**: 523-553 (Sept.) 1938; Studies on Experimental Hypertension: XII. The Experimental Production and Pathogenesis of Hypertension Due to Renal Ischemia, Am. J. Clin. Path. **10**: 40-72 (Jan.) 1940.

4. Aschoff, L.: Pathologische Anatomie: Ein Lehrbuch für Studierende und Ärzte; Spezielle pathologische Anatomie, Jena, G. Fischer, 1909, vol. 2.

5. Haslinger, K.: Die pyelonephritische Schrumpfniere, Ztschr. f. urol. Chir, **24**: 1-83, 1928.

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7. Fahr, T.: Über pyelonephritische Schrumpfniere und hypogenetische Nephritis, Arch. path. Anat. **301**: 140-185, (Jan.) 1938.

8. Linder, F.: Beitrag zur pathologischen Anatomie der pyelonephritischen Schrumpfniere unter besonderer Berücksichtigung ihrer Arterienveränderungen, Frankfurt, Ztschr. f. Path. **51**: 150-170, 1937.

9. Lieberthal, F.: Pyelonephritic Contracture of the Kidney, Surg., Gynec. & Obst. **69**: 159-171 (Aug.) 1939.

of hypertension and results of nephrectomy in cases of unilateral renal "atrophy" has already been evaluated accurately by others, we decided to include this phase of the subject in this study. Because of this, we eliminated from the study all cases in which bilateral lumbar sympathectomy had been done in addition to nephrectomy for relief of hypertension. We did not eliminate the patients who had undergone unilateral sympathectomy, as it is now well known that this limited procedure is not effective in the treatment of hypertension.

This left for study a total of 183 cases of unilateral renal "atrophy" in which the etiological agent was not readily apparent. The group included a typical variety of cases such as are seen in any urology clinic and which usually are diagnosed as "atrophic pyelonephritis or congenital hypoplasia." In 79 of these 183 cases, nephrectomy had been performed, so that the pathological specimen was available for gross and microscopic study.

A further word of explanation should be said here concerning the selection of cases for this study. Although many of these cases are included in the studies of Braasch and associates [10] and Barker and Walters [11] concerning nephrectomy for hypertension in unilateral renal disease, the two groups of cases cannot be compared. The reason for this is that we eliminated many cases in which the cause of the lesion, such as obstruction and stone, was apparent or associated lesions were present. Such cases are important factors in hypertension, so that, because of their elimination, one would not expect our figures for the incidence of hypertension, results of nephrectomy, and the like, to be similar to theirs.

Definition of "Atrophy." — We might logically be asked on what basis we decided that a kidney was sufficiently reduced in size to be called "atrophic." In the nonsurgical cases the decision was made on the basis of urography. If the kidney seemed to be less than two-thirds the size of its mate, we included it in the study. In the surgical cases the selection was made on the basis of weight. Most authoritative tables give the weight of the normal adult kidney as between 140 and 150 gm. We included all kidneys that weighed less than 100 gm. In the tables that deal with this problem (tables 3 and 5) we denoted the degrees of "atrophy" of a kidney as follows: grade 1 "atrophy," weight 76 to 99 gm.; grade 2, 51 to 75 gm.; grade 3, 26 to 50 gm.; and grade 4, 25 gm. or less. As a matter of fact, only three kidneys in the surgical group weighed more than 75 gm. All kidneys were weighed without the perirenal fat.

There is an obvious discrepancy in this arbitrary grading if infants and children are considered. Most accepted tables state that the kidney of an infant aged 1 year weighs about 20 gm. The weight of the kidney gradually increases with age, so that at the age of 10 years the average weight is about 96 gm. In our series of surgical cases there were three patients less than 10 years of age, as follows: 1 year, 6 years, and 7 years. The respective weight of the kidney removed from each was as follows: 14 gm., 9 gm., and 7.5 gm.

10. (*a*) Braasch, W. F.: Genitourinary Surgery: Renal Disease as a Factor in Hypertension, Am. J. Surg. **56**: 209-215 (April) 1942; The Surgical Kidney as an Etiological Factor in Hypertension, Canad. M. A. J. **46**: 9-15 (Jan.) 1942. (*b*) Braasch, W. F.; Walters, W., and Hammer, H. J.: Hypertension and the Surgical Kidney, J. A. M. A. **115**: 1837-1841 (Nov. 30) 1940. (*c*) Barker, N. W., and Braasch, W. F.: Collective Review: The Course of Hypertension After Nephrectomy for Advanced Unilateral Renal Disease, Internat. Abstr. Surg. **84**: 299-304 (April) 1947. (*d*) Braasch.[3]

11. Barker, N. W., and Walters, W.: Hypertension and Chronic Atrophic Pyelonephritis: Results of Nephrectomy J. A. M. A. **115**: 912-916 (Sept. 14) 1940.

ANALYSIS OF MATERIAL

Data Concerning Entire Group of 183 Cases.—Age and Sex Incidence: Almost two-thirds of the patients were women. The commonest age period was from 21 to 50 years, although the condition was encountered in all ages.

Evidence of Present or Past Infection: Inasmuch as one of the most controversial points that we are trying to settle is whether differentiation between "congenital hypoplasia" and chronic "atrophic pyelonephritis" is possible, we divided the 183 cases into two groups: A and B. In group A we have put all those cases in which history or findings even remotely suggest any possible renal infection, past or present. As evidence for present infection we made the following stipulations:

Male	Voided vesical urine: more than 20 leukocytes per high power field Catheterized urine: 5 or more leukocytes per high power field
Female	Voided vesical urine: more than 50 leukocytes per high power field Catheterized urine: 20 or more leukocytes per high power field
Male and female	3 or more leukocytes per high power field in ureteral specimen of urine

As evidence of past infection we admitted a history of attacks of pyelitis or pyelonephritis, a history of chills, fever, perinephric abscess, renal pain, dysuria (especially in infancy), and a history of "pus in the urine." When in doubt, we placed the patient in group A, so that, so far as possible, the patients in group B should have or have had little chance for previous or present gross infection. The only patients put in group B who had urinary symptoms were those with normal urine in whom a satisfactory explanation of vesical symptoms was found, such as enlarged prostate gland, cystocele, and chronic urethritis in women. For the remainder of the analysis of this group of 183 cases, therefore, they will be divided into groups A and B. In group A will be found 115 cases, while only 68 are put in group B. Of the 115 cases in group A, ureteral specimens of urine from the "atrophic" kidney were available in only 74. Of these 74 there was evidence of infection (more than 3 leukocytes per high power field) in only 25 (approximately a third).

Incidence of Hypertension: The commonest signs and symptoms associated with the unilateral "atrophic" kidney are hypertension and renal pain. The incidence of hypertension is considered in table 1. In this study we have defined hypertension as a blood pressure of 150 mm. of mercury systolic and 100 diastolic or more. If either reading was lower than these figures, the condition was not regarded as hypertension. If two or more readings were available, the lowest was used. The incidence of hypertension for the entire group was 37%. This is somewhat lower than the figure of approximately 45% suggested by Braasch. This difference, however, is no doubt due to the fact that we have eliminated so many cases complicated by such conditions as obstruction and stone, as explained previously. The incidence of hypertension in group B is higher than in group A. This may or may not be of significance.

We found that about half the patients complained of pain that could possibly be interpreted as being of renal origin. In many cases, however, the pain was mild and difficult to distinguish from an ordinary backache.

Role of Renal Function: The functional ability of the "atrophic" kidney is an important subject. It has become a frequent topic for discussion, many articles on the subject being written primarily to warn surgeons against removing a kidney for any reason without first adequately demonstrating that the remaining kidney is not "atrophic" and incapable of supporting life. An analysis of renal function is made in table 2. Any estimate of renal function is admittedly inaccurate but nevertheless very important. In most cases we have made our estimate on the basis of the excretory urograms; however, in a few cases additional data from phenolsulfonphthalein or indigo carmine excretion were available. It will be noted that only 55 (about 30%) of the "atrophic" kidneys showed evidence of "normal" function, while 76 (about 42%) showed poor or no function to be present. This is in contrast with the opposite kidney, in which normal function was estimated in more than 90% of cases. The minor differences between the two groups (A and B) do not appear to be significant.

Data Concerning the 79 Surgical Cases in Which Nephrectomy Was Performed.—As previously stated, in 79 of the 183 cases nephrectomy was done, so that the "atrophic" kidney was available to us for study. These 79 cases will now be considered as a separate group for analysis. The sex incidence was essentially the same as for the larger group. These cases were divided into A and B groups (see footnotes to table 1), and analyzed with respect to the incidence of hypertension, presence or absence of infection in the ureteral specimen of urine, and the grade of "atrophy" of the kidney. Forty-eight cases were in the A group, while 31 were in the B group. Of the 40 ureteral specimens of urine available for study in the A group, only 16 (40%) showed pyuria (more than 3 leukocytes per high power field). These findings further emphasize the difficulty of deciding clinically the importance of infection as a factor in renal "atrophy."

Incidence of Hypertension: Of the 79 cases, 43 (54%) had associated hypertension. This is a higher incidence than for the entire group (37% of 183 cases). Here again the explanation of this apparent discrepancy probably lies in the fact that the commonest indication for nephrectomy in renal "atrophy" is hypertension. Therefore, one would expect a higher incidence in a group of cases in which operation had been performed than in cases in which operation had not been performed. Further breaking down of the figures showed that the incidence of hypertension in the group B cases (without infection) was considerably greater than in the group A cases.

Incidence of Hypertension Correlated with Degree of Renal "Atrophy": The degree of renal atrophy apparently has little or nothing to do with the incidence of hypertension, since, oddly enough, there was a greater incidence (approximately 90%) of grade 3 and grade 4 "atrophy" in group A than in group B (approximately 71%), which had the higher incidence of hypertension. The fact that the majority of kidneys removed were of grade 3 or 4 "atrophy" probably has no great clinical significance, because most clinicians tend to urge nephrectomy for hypertension only in patients who have very definite and advanced renal "atrophy."

Indications for Nephrectomy: An analysis of the 79 cases showed that nephrectomy was advised for two principal reasons: renal pain and hypertension.

Results of Nephrectomy: Relief of pain. Because of inadequate follow-up notes on the histories, it was not always possible to estimate with accuracy the degree of relief secured from renal pain (which often was very mild). It was our impression, however, that good results were achieved in the majority of cases.

TABLE 1.—*Incidence of Hypertension in 183 Cases of "Atrophic" Kidney*

Group	Age, Yr.	Total Cases	Cases with Hypertension, No.
A *	0-10	3	1
	11-20	10	3
	21-30	26	2
	31-40	29	13
	41-50	20	4
	51-60	18	10
	61 or more	9	4
Subtotal		115	37 (32%)
B †	0-10	3	1
	11-20	4	3
	21-30	15	7
	31-40	16	9
	41-50	20	7
	51-60	5	2
	61 or more	5	2
Subtotal		68	31 (46%)
Grand total		183	68 (37%)

* Group A: Cases with evidence of past or present infection. See text for explanation.

† Group B: Cases with no evidence of past or present infection. See text for explanation.

TABLE 2.—*Analysis of the Status of Renal Function in 183 Cases of "Atrophic" Kidney*

Group	Total	Degree of Function, No. of Cases				
		Normal	Fair	Poor	Absent	Not Determined
A	115	29	31	29	20	6
B	68	26	13	12	15	2
Total	183	55	44	41	35	8

Relief of hypertension. In evaluating the results of nephrectomy for hypertension, we have established the same arbitrary definitions as those used by Barker and Braasch [10c]: (1) good, denoting that the systolic pressure decreased to less than 150 mm. of mercury and the diastolic pressure to less than 100, (2) fair, if the blood pressure was significantly reduced, but still was 150 mm. of mercury systolic and 100 diastolic, or more, and (3) poor, denoting no significant reduction in blood pressure. Immediate good results (table 3) were obtained in 22 of the 43 cases (approximately 50%). This is almost an identical figure with that of Barker and Braasch for the results in unilateral renal disease in general but slightly higher than for their smaller group of selected cases of "atrophic pyelonephritis," in which there were approximately 41% good results. The results seem to be slightly better in group B than in group A, but the number of cases in each group is too small to be of statistical significance.

A word should be said about the permanence of results. Five of the 43 patients were not traced in the two-year or more period. Of the 22 patients with immediate good results, 19 maintained these good results, but the other 3 dropped to "fair" in the two-year follow-up. All the patients who secured fair immediate results maintained them in the two-year follow-up except for one patient who was not traced. Because of the fact that only such a small percentage of patients do not maintain their immediate results, in the subsequent analysis we shall employ only the immediate postoperative results in our comparison and correlations.

Results of Nephrectomy Correlated with Duration of Hypertension and Results of Funduscopic Examination: It is impossible to secure accurate information concerning the duration of hypertension. Many patients are not aware of its presence until they are examined for advanced late symptoms of this disease. Even though such information is inaccurate, we have included it in table 4, where we have recorded the "known" duration of hypertension and compared it with the results of nephrectomy. Although the table suggests that the best results are achieved in patients in whom the duration of hypertension is less than five years, it must be remembered that many such patients may have had the disease many more years than had been realized. The same generalizations can be made in regard to pathological changes found in the eye grounds (table 4). Although it appears that the majority of good results occurs in those cases with minimal (group 1 or 2) changes (Keith-Wagener classification [12]), good results are achieved in patients with advanced retinopathy (groups 3 and 4).

Results of Nephrectomy Correlated with Degree of Renal "Atrophy": This information is also given in table 4. There is no correlation between the weight of the kidney and the result of nephrectomy.

Results of Nephrectomy Correlated with Age of Patient: We compared the results of nephrectomy with the patients' ages by decades. There seems to be no correlation.

Pathological Study of the 79 Surgical Cases.—Up to this point it seems apparent that none of the clinical data accumulated so far in this study are of much value in the solution of our problem: Are there two definite entities (chronic "atrophic" pyelonephritis and congenital hypoplasia) and, if so, may they be differentiated with accuracy? We now turn to the gross and microscopic examination of the kidneys in search of an answer.

Pathological Classification: The pathological examination was undertaken in an entirely objective manner, each kidney being examined without any knowledge of the clinical or urographic data associated with it. Specimens were examined both grossly and microscopically. In the gross specimen we looked especially for depressions and irregularity of the surface (caused by scars) and difficulty in stripping of the capsule from the kidney. Lack of uniformity of thickness of the cortex, we felt, was also suggestive. For the microscopic study, slides were made from radial sections cut from both the most and the least affected areas of our specimens, in an attempt to include all histological elements from the renal cortex to the papillae. Slides were stained with hematoxylin-eosin and van Gieson stains.

The chief object of the pathological examination was to see whether there were features (either gross or microscopic) that would permit segregation of specimens into separate groups or classifications. This study proved most disheartening. The further the examination proceeded, the more it became apparent that grouping or classification was impractical if not wholly impossible. Nevertheless, in an effort to explore all possibilities exhaustively, the kidneys were placed in four groups on the basis of rather meager and unconvincing pathological data, so that they could be compared with clinical and urographic data. The four groups were as follows: (1) aplasia, (2)

TABLE 3.—*Results of Nephrectomy for Hypertension (Forty-Three Cases) of "Atrophic" Kidney*

Result	Time After Operation: Immediate (2 to 4 Weeks) Total	Immediate (2 to 4 Weeks) Group A	Immediate (2 to 4 Weeks) Group B	2 Yr. or More Total *	2 Yr. or More Group A	2 Yr. or More Group B	5 Yr. or More Total †	5 Yr. or More Group A	5 Yr. or More Group B
Good	22	8	14	19	6	13	8	2	6
Fair	7	4	3	9	5	4	5	2	3
Poor	13	7	6	7	4	3	2	1	1
Unknown	1	1	..	..	..	..	..	..	..
Dead	..	..	..	3	1	2	3	1	2
Not traced	..	..	..	5	3	2	25	..	..
Total	43			43			43		

* Traced patients. † Some patients were not traced; others have been traced for less than a five-year period.

TABLE 4.—*Analysis of Forty-Three Cases, Groups A and B, with Hypertension*; Immediate Results as Correlated with Duration of Hypertension, Status of Fundus, and Grade of Contraction of Kidney*

Results	Total Cases	Known Duration of Hypertension: 0-5 Yr.	5-10 Yr.	10 Yr. or More	Not Known	Status of Fundus, Grading of Changes (Keith-Wagener): 0	1	2	3	4	Grade of Contraction of Kidney: 1	2	3	4
Good	22	19	2	1	..	..	11	5	2	4	2	6	4	10
Fair	7	3	2	2	..	..	1	3	3	..	..	1	5	1
Poor	13	5	4	3	1	..	8	3	2	..	1	3	4	5
Unknown	1	1	..	..	..	..	..	1	..	..	..	..	..	1

* With or without infection or history of infection.

12. Wagener, H. P., and Keith, N. M.: Diffuse Arteriolar Disease with Hypertension and the Associated Retinal Lesions, Medicine **18**: 317-430 (Sept.) 1939.

congenital hypoplasia, (3) chronic "atrophic" pyelonephritis, and (4) chronic "atrophic" pyelonephritis superimposed on congenital hypoplasia.

Aplasia: For this group we stipulated as an arbitrary definition of renal aplasia that no functioning renal tissue exists. Grossly the tissue does not appear as a kidney.

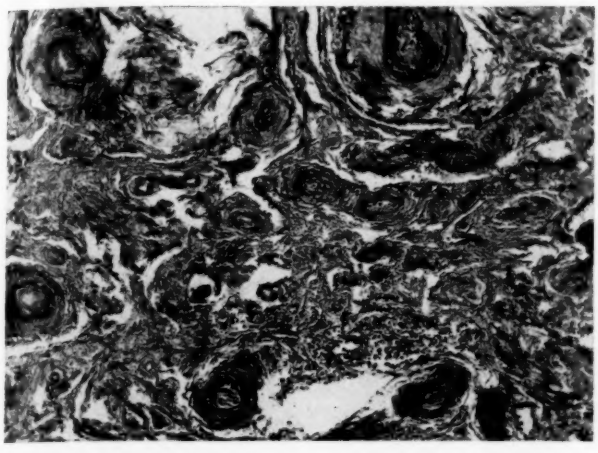

Fig. 1.—Aplasia of the kidney. The kidney is represented by a few tubules, without glomeruli. Note the marked endarteritis (van Gieson).

Usually one finds a mass of fibrous tissue, within which are embedded a few cystic tubules. (If any glomeruli were seen, the case was put in the group of hypoplasias rather than aplasia.) Of the six cases in this group the ureter could not be catheterized in five, a fact that would indicate the accuracy of Gutierrez' statement that the ureter usually is incompletely developed and not patent.

In our cases usually there was a definite renal pedicle present, which contained the usual structures. We were impressed with the findings of intimal thickening in the large vessels in the pedicle (fig. 1), which we feel is probably in the nature of physiological endarteritis. (This

Fig. 2.—The scarring in the kidney probably represents the second stage of pyelonephritis. There is marked endarteritis (van Gieson).

process is also seen in the iliac artery to a limb that has been amputated years before, or in a branch of the pulmonary artery when the lobe of the lung supplied by it has been functionless over a long period.) It has been a common concept that intimal thickening does not occur in hypoplasia or aplasia of the kidney, but this has been contrary to our findings. It would appear, therefore, that endarteritis is of little value in defining the various types of lesions that produce a small "atrophic" kidney. Six of our 79 surgical cases were included in the aplastic group.

Congenital Hypoplasia: This posed a more difficult problem than aplasia for pathological evaluation. Again, by our own arbitrary definition a kidney put in this group is small, but it is a functioning kidney containing normally functioning glomeruli and tubules. The normal contour of the kidney was usually preserved, although fetal lobulations were frequently present. Vascular changes were not prominent. Inasmuch as most of these kidneys had been catheterized shortly before nephrectomy was done, there were multiple foci of inflammatory cells, and in many cases small abscesses were present. (This finding has been noted in our pathology laboratory for years, in kidneys removed at operation that had been

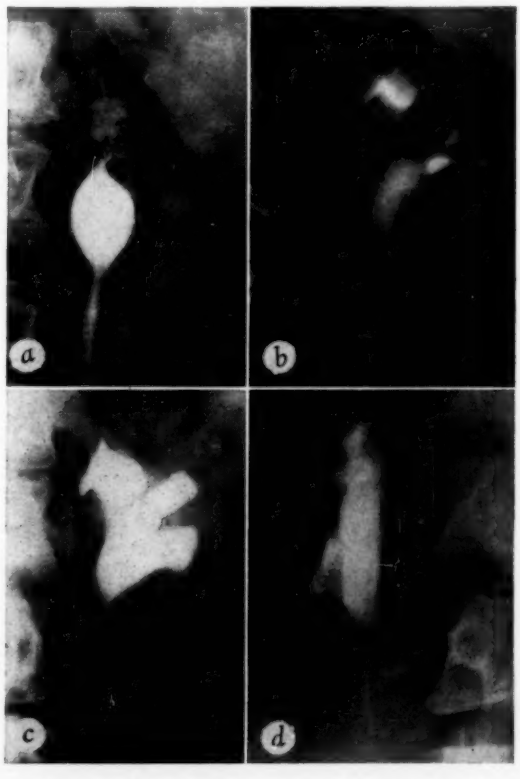

Fig. 3.—Varieties of pyelograms encountered in "atrophic" kidneys. The "pathological classification" (see text) of the illustrations is as follows: *a*, renal aplasia; *b*, *c*, and *d*, congenital hypoplasia.

catheterized cystoscopically shortly before operation.) This finding increases the difficulty of distinguishing between congenital hypoplasia and chronic "atrophic" pyelonephritis. We were not able to substantiate the statement that frequently appears in the literature to the effect that there are fewer pyramids in this type of kidney than in the normal kidney. All of our material was fixed, and the accurate identification of pyramids did not seem feasible. Nine of our 79 surgical cases were included in the hypoplastic group.

Chronic "Atrophic" Pyelonephritis: It is well known that obstruction with infection and subsequent hydronephrotic atrophy is a common cause of renal atrophy. We have tried to exclude all such cases that in any way demonstrated obstruction or hydronephrosis. In the cases put in this group we observed primarily scars (gross or

microscopic), which were presumably the result of infection. There was often hyalinization of the glomeruli in the scarred areas, together with cystic dilatation of the tubules. In some cases there were collections of lymphocytes and other inflammatory cells, but in others none were apparent (indicating, we thought, a "burned-out" infection). Vascular changes in the scarred areas consisted of intimal thickening of the medium-sized vessels with resultant narrowing of the lumen (fig. 2). This finding is not helpful in differential diagnosis, because the vessels of the same size are affected in the arteriosclerotic kidney (other terms: nephrosclerosis, benign nephrosclerosis). Malignant nephrosclerosis and chronic glomerulonephritis are more easily excluded, because in these cases the small vessels and arterioles are involved diffusely and the lesion usually is bilateral. Fifty-one of the 79 surgical cases were included in this group of cases of chronic "atrophic" pyelonephritis.

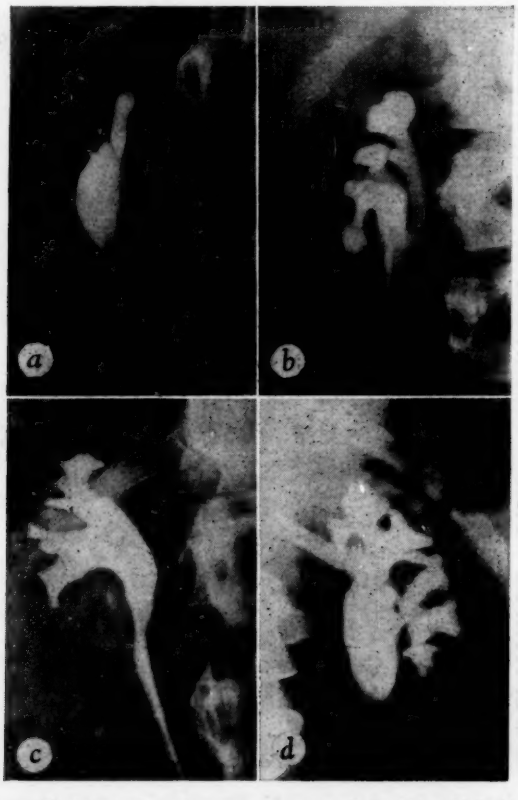

Fig. 4.—Varieties of pyelograms encountered in "atrophic" kidneys. The "pathological classification" (see text) of the illustrations is as follows: *a*, congenital hypoplasia; *b*, *c*, and *d*, congenital hypoplasia with superimposed chronic pyelonephritis.

Chronic "Atrophic" Pyelonephritis Superimposed on Congenital Hypoplasia: In this category were placed cases in which a portion of the kidney did not show scars, a fact which suggested that the kidney had always been a small one. In this type of case part of the kidney showed scarring with narrowing of the cortex. Histological study of the unscarred portion of the kidney revealed no increased fibrous tissue, inflammatory cells, or vascular changes, while the scarred portion revealed those three features. It is interesting to speculate as to how many "atrophic" scarred kidneys are the result of infection engrafted on a comparatively small kidney. Thirteen of the 79 surgical cases were included in this group.

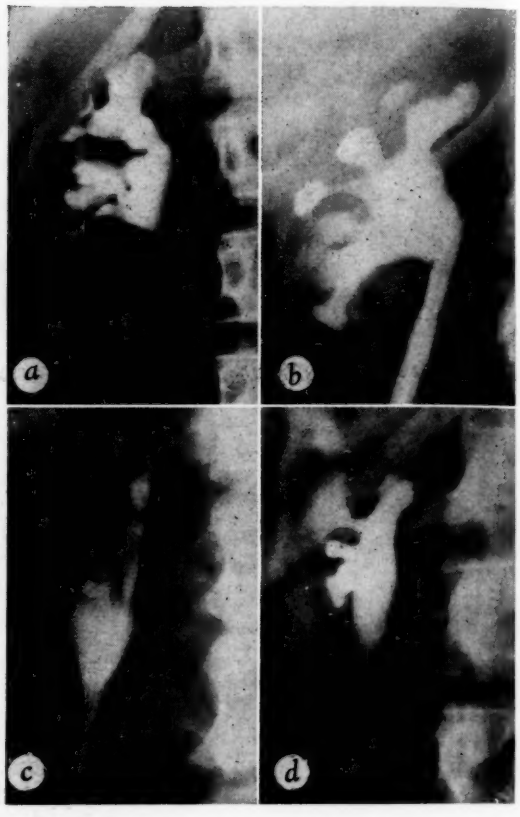

Fig. 5.—Varieties of pyelograms encountered in "atrophic" kidneys. The "pathological classification" (see text) in *a*, *b*, *c*, and *d* is chronic atrophic pyelonephritis.

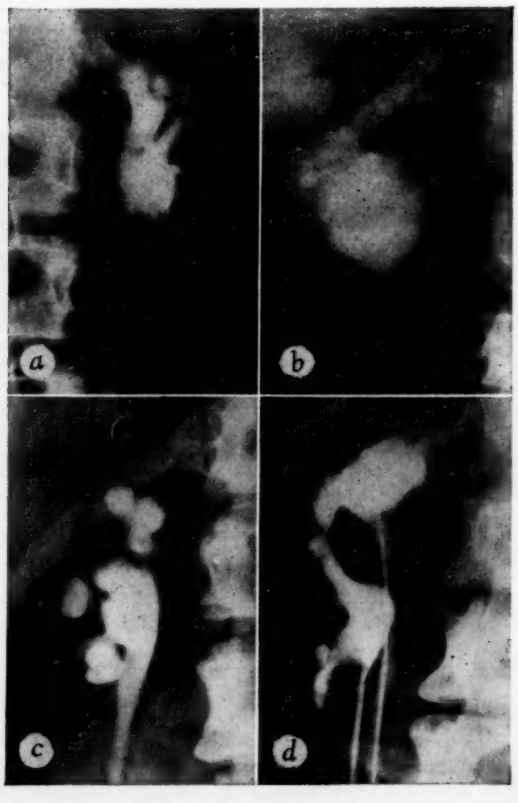

Fig. 6.—Varieties of pyelograms encountered in "atrophic" kidneys. The "pathological classification" (see text) in *a*, *b*, *c*, and *d* is chronic atrophic pyelonephritis.

Pathological Classification Correlated with Age, Incidence of Hypertension, and Evidence of Infection: As can be surmised from our description of the pathological study, we were not impressed with our ability to classify and distinguish varieties of renal "atrophy" or hypoplasia. Having made an attempt at classification, however, it seemed worth while to further attempt to assess its value. In table 5 our four pathological classifications have been compared with age, incidence of hypertension, and evidence of infection. It can be seen that there is no correlation with the age of the patient. There seems to be no significant correlation between the incidence of hypertension and the various pathological groups, and, to further discourage attempts at classification, of the four ureteral specimens available in the hypoplastic group, three showed gross infection. To confuse the issue further, only 12 of the 29 available ureteral specimens of urine in the chronic "atrophic" pyelonephritis group contained pus cells.

Pathological Classification Correlated with Results of Nephrectomy for Hypertension: In table 6 it can be seen that apparently there is no correlation between the pathological diagnosis and the results that can be noted from nephrectomy in the patients with hypertension.

TABLE 5.—*Correlation of Pathological Classification in Seventy-Nine Surgical Cases of Renal "Atrophy" with Age, Incidence of Hypertension, and Evidence of Possible Previous or Present Infection*

Pathological Classification	Total Cases	Age, Yr.			With Hypertension		Possible Evidence of Past or Present Infection		Ureteral Specimens Available, No. of Cases	Pus Present, More than 3 Leukocytes per High Power Field, No. of Cases
		0-20	21-40	41+	No. of Cases	%	No. of Cases	%		
Aplasia	6	..	3	3	1	17	2	33	2	0
Hypoplasia	9	1	4	4	4	44	6	67	4	3
Hypoplasia and chronic "atrophic" pyelonephritis	13	3	7	3	7	54	6	46	5	1
Chronic "atrophic" pyelonephritis	51	10	24	17	31	61	34	67	29	12

Role of Pyelography in the "Atrophic" Kidney.—Inasmuch as definite statements have appeared in the literature concerning the many varieties of pyelographic deformity seen in the various types of hypoplasia and "atrophy," we decided to try to evaluate this phase of the problem. We critically reviewed the urograms in all 79 surgical cases and listed all findings that could be considered to fit definite descriptive terms. Among the commoner findings could be listed (1) the vertical pelvis, (2) pelvis lying close to spinal column, (3) inflammatory changes in the calyces, (4) "bizarre" type of calyces, and (5) evidence of minimal degrees of pyelectasis and caliectasis. Among the less frequent descriptions were listed such things as (1) pelvis and calyces larger than one would expect for the size of the renal cortex, (2) size of pelvis and calyces corresponding to size of renal cortex, (3) no major calyces, and minor calyces appearing to arise directly from the pelvis, and (4) absence of calyces.

TABLE 6.—*Correlation of Pathological Diagnosis in Forty-Three Patients with Hypertension and Results (Immediate) of Nephrectomy*

Pathological Classification	Total Cases	Results			
		Good	Fair	Poor	Not Known
Aplasia	1	..	..	1	..
Hypoplasia	4	2	..	2	..
Hypoplasia and chronic "atrophic" pyelonephritis	7	4	3	..	..
Chronic "atrophic" pyelonephritis	31	16	4	10	1

All these findings were charted against such factors as the pathological classification (e. g., aplasia or hypoplasia and chronic "atrophic" pyelonephritis) and clinical grouping (groups A and B), and absolutely no correlation could be found. In our opinion any type of pyelogram found in this study can occur in any of the arbitrary classifications or groups that we have been able to create. To illustrate this point, we have reproduced here 16 typical pyelograms and have indicated the pathological groups in which they occurred (fig. 3, 4, 5, and 6).

SUMMARY AND CONCLUSIONS

There is no doubt in our minds that the unilateral "hypoplastic" or "atrophic" kidney represents several different and distinct pathological entities. We are sure that in some cases the lesion is congenital, while in others it is the result of acquired or a combination of congenital and acquired conditions. One of the commonest acquired conditions is infection ("chronic atrophic pyelonephritis"). We feel that in some cases of apparent chronic "atrophic" pyelonephritis the kidney may have been congenitally small to start with, but we know of no way to decide this problem accurately.

Among other acquired conditions that predispose to "atrophy" may be mentioned obstruction (with or without infection), complete or partial vascular occlusion, infarcts, and stone (with or without infection). Primary vascular disease, such as benign and malignant nephrosclerosis and glomerulonephritis, may be the underlying cause in some cases, but this usually is a bilateral lesion. Our study indicates that it is impractical and almost impossible to attempt to distinguish these conditions—clinically, pathologically, or urographically—with any degree of accuracy.

Although the unilateral hypoplastic or "atrophic" kidney is of importance as a cause of hypertension, as near as we can ascertain, the incidence of hypertension and the results of nephrectomy are approximately the same in every artificial group that we have been able to create (clinically, pyelographically, or pathologically). For this reason it would seem that it might be more sensible to forego any attempts at classification according to origin and clinical findings and instead to employ some common "blanket" term, such as "atrophic kidney" or "renal atrophy," to describe the unilateral small kidney, the cause of which is not apparent.

ANTIBIOTICS AND LOW CERVICAL CESARIAN SECTION IN DYSTOCIA OR INTRAPARTUM SEPSIS

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The low cervical cesarian section may be safely employed in the presence of sepsis. This statement is supported by 140 consecutive transperitoneal cesarian sections without a fatality in patients who were either potentially or actually infected. This has been accomplished by the addition of modern chemotherapy.

TRANSPERITONEAL CESARIAN SECTION VERSUS EXTRAPERITONEAL CESARIAN SECTION

Prior to the advent of modern antibacterial therapy a succession of cesarian section techniques was developed. Each supplanted the previous ones, and all made claims of superiority in minimizing postoperative sepsis. The cesarian hysterectomy, for purposes of preventing or controlling postoperative sepsis, has lost most of its adherents. A substantial number of physicians still prefer the extraperitoneal cesarian techniques when infection threatens or is actually present. Almost simultaneous with the current revival of the extraperitoneal operations came the availability of effective chemotherapy. Sulfonamides and penicillin and other more recent antibiotics were found to be highly efficient, when used conjointly, in combating such forms of infection as postoperative peritonitis and puerperal sepsis. The advocates of extraperitoneal cesarian section thereupon included this form of protection against sepsis but, nevertheless, maintain it is particularly the surgical procedure that enables the septic patient to recover.[1] We saw no difference in the results of our extraperitoneal cesarian sections, regardless of whether the peritoneum was accidentally opened. In fact, one patient on whom an elective extraperitoneal cesarian section was performed had severe postoperative sepsis and ileus, even though the peritoneal cavity was not disturbed. Mengert [2] has cited a maternal death following an extraperitoneal cesarian section in which autopsy revealed peritonitis but no peritoneal injury. It is therefore doubtful that this technique could be the intrinsic source of the better postoperative results.

Recently Settle and Wilson,[3] Portes and Mayer,[4] Perez,[5] Douglas and Landesman,[6] McDonald,[7] Bazan and his associates,[8] and Dantuono [9] advocated the low cervical cesarian section when the patient's resistance is bolstered by the protective administration of antibacterial agents. In the cases they reported the patients had prolonged labors and ruptured membranes for many hours. Heretofore the danger of severe postoperative sepsis and maternal death virtually contraindicated transperitoneal cesarian sections in such patients. The acid test for the efficacy of chemotherapy is its application in conjunction with the low cervical cesarian in patients having intrapartum sepsis. Recently we reported a study [10] of 100 low cervical cesarian sections performed on such patients. Previously they would probably have been subjected to a cesarian hysterectomy or an extraperitoneal cesarian section, or, possibly, a mutilating operation would have been performed on a dead fetus. Forty-seven patients with intrapartum sepsis were included in this report, and five of these had been in labor for a long period before admission to our service. The results were no maternal deaths, a surprisingly mild recovery in most instances, and no postoperative peritonitis; this could leave no other conclusion but that this new trend in the management of septic or potentially infected patients during labor has a valid basis for its continuation.

PROLONGED LABOR AS RELATED TO CESARIAN SECTION

The incidence of prolonged labor (24 hours or longer) at the Cook County Hospital is 1 to 2%. When it was demonstrated that use of penicillin combined with sulfonamides (and occasionally streptomycin) assured the recovery of patients unable to be delivered otherwise, the incidence of transperitoneal cesarian sections reached 15% in cases of prolonged labor. In the past three years the incidence of low cervical cesarian sections among patients potentially or actually infected amounted to approximately 0.3% of all patients delivered in the Cook County Hospital Obstetrical Services.

Obstetric judgment in its finest form is needed when dystocia is present. To begin with, it is not easy to foretell dystocia when obvious fetopelvic disproportions and malpresentations have been screened out. Furthermore, constriction ring dystocia is more prevalent in these cases. A borderline disproportion in itself is difficult to diagnose, but, when masked by the presence of dysfunctional uter-

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From the Obstetrical Departments of the Cook County, Mt. Sinai, and Edgewater hospitals and the Departments of Obstetrics and Gynecology of the University of Illinois, the Chicago Medical School, and Northwestern University.

1. Cosgrove, S. A., and Waters, E. G.: Evaluation of Extraperitoneal Cesarean Section, Am. J. Obst. & Gynec. **52**: 237 (Aug.) 1946. McCall, M. L.: Extraperitoneal Cesarean Section in the Profoundly Infected Patients, ibid. **57**: 520 (March) 1949.

2. Mengert, W. F.: in discussion on Diekmann, W. J.; Bjork, F. J., and Aragon, G. T.: Cesarean Hysterectomy at the Chicago Lying-In Hospital, J. A. M. A. **137**: 1017 (July 17) 1948.

3. Settle, J. M., and Wilson, L. A.: Cesarean Section in Potentially Infected Patients Using Sulfathiazole in Uterus and Peritoneal Cavity, Am. J. Obst. & Gynec. **54**: 801 (Nov.) 1947.

4. Portes, L., and Mayer, M.: Note sur l'emploi de la pénicilline dans les opérations Césariennes en cas d'infection amniotique, Gynec. et obst. **45**: 508, 1946; abstracted, Year Book of Obstetrics and Gynecology, Chicago, The Year Book Publishers, Inc. 1947, p. 178.

5. Perez, M. L.: Les Sulfamides par voie intra-péritonéale a titre prophylactique dans la chirurgie obstétricale des cas impurs, Gynec. et. obst. **46**: 5, 1947; abstracted, Year Book of Obstetrics and Gynecology, Chicago, The Year Book Publishers, Inc., 1947, p. 179.

6. Douglas, R. G., and Landesman, R.: Sulfadiazine and Penicillin Prophylaxis in Cesarean Section, Am. J. Obst. & Gynec. **56**: 422 (Sept.) 1948; Recent Trends in Cesarean Section, ibid. **59**: 96 (Jan.) 1950.

7. McDonald, R. P.: Reevaluation of Low Cervical Cesarean Section, Texas J. Med. **44**: 460 (Oct.) 1948.

8. Bazan, J.; Uranga Imaz, F. A., and Schiavo, C. D.: La cesarea en el caso impuro (a través de 1138 observations), Bol. Soc. obst. y ginec. Buenos Aires **27**: 571, 1948.

9. Dantuono, L. M.: Cesarean Section After Prolonged Labor: Influence of Prophylactic Sulfonamide and Penicillin Therapy on Operative Procedure and End Results, Am. J. Obst. & Gynec. **60**: 1298 (Dec.) 1950.

10. Kobak, A. J.; Fields, C., and Turow, D. D.: Prophylactic Chemoantibiotic Therapy and Low Cervical Cesarean Section in Potential and Actual Infections, Am. J. Obst. & Gynec. **60**: 1229 (Dec.) 1950.

ine action, it becomes a challenge to the obstetrician. Roentgenographic pelvimetry is of questionable value. McKelvey,[11] a proponent of this type of mensuration, has pointed out that the information thus obtained cannot decisively separate patients who will need a cesarian section from those certain to deliver vaginally. There is a doubtful range in all planes of the pelvis that prevents such precision. With the application of antibacterial agents, a full test of labor can now be given without nullifying the safety of a transperitoneal cesarian section when it later becomes necessary. The following two cases exemplify this.

CASE 1.—M. W., a white primigravida, 17, had an artificial rupture of the membranes after 30 hours of labor. The cervix was completely dilated in 34 hours. Three attempts at forceps delivery were unsuccessful. It was then noted that the head fitted the bony pelvis very tightly. Roentgenographic pelvimetry revealed the transverse of the midplane to be 9.1 cm. The patient was delivered by a low cervical section after 42 hours of labor. She had fever for two days, with a peak of 102 F on the day of delivery. The patient left the hospital on the 16th day with her baby, who weighed 7 lb. 5½ oz. (3,340 gm.) at birth. She was in good condition.

CASE 2.—M. S., a white primigravida, 29, was told by an orthopedic surgeon that her pelvis was not normal. A roentgenogram of her pelvis during gestation was reported as showing "spondylolisthesis of the first degree." The attending obstetrician could not corroborate this digitally, and it was decided, therefore, to give the patient a test of labor. The membranes ruptured two hours before the onset of labor. The cervix was completely dilated in 19½ hours. After two hours of good contractions with no progress, a vaginal examination revealed that the head was tightly pressed against the bony portion of the midpelvis, with the dependent portion of the presenting fetal head at 2+ to 3+ station. The patient was thereupon scheduled for an abdominal delivery, but the operation had to be delayed until the completion of a surgical emergency that was scheduled earlier. Thus a low cervical cesarian section was performed with the patient under spinal anesthesia after 25 hours of labor. The patient received penicillin and streptomycin preoperatively and postoperatively. There was no postoperative morbidity, and on the ninth day the patient was discharged with a normal baby, who weighed 7 lb. 15 oz. (3,630 gm.) at birth.

Women infected and neglected still come to our obstetric service for delivery, despite medical education in maternal welfare and community teaching.[12] Patients who have prolonged labor and whose labor continues for long periods after rupture of the membranes become potentially or actually infected.[13] Regardless of the ultimate manner of delivery, the obstetrician must be mindful of keeping the patient in the best possible condition. For this purpose periods of rest by sedation and fluid balance maintenance are very helpful. Dehydration and acidosis in the course of prolonged labors are factors in causing temperature elevation. Blood transfusions are particularly valuable for increasing the patient's chances for recovery. The anesthesia must also be carefully selected in the best interests of both the parturient and the fetus. In addition to such supervision, the patient receives chemotherapy prophylactically as soon as dystocia labor is regarded as even a remote possibility.

The decision to perform an abdominal delivery should be made when it is obvious that labor is not progressing. This can be due to borderline pelvic disproportion or to the association of other factors, such as malpresentation or the development of a constriction ring. Dysfunctional uterine action frequently accompanies the foregoing complications, but it also can be the only obvious reason for the prolonged labor. In the latter instance, rupture of the intact membranes is indicated. If this does not improve the contractile action of the uterus satisfactorily, oxytocin injection (pitocin®) may be given hypodermically in small doses repeated every 20 minutes, or intravenously in a highly diluted mixture.[14] Failure of oxytocics to bring about an effective uterine action occasionally occurs; if this happens, a cesarian section should be done if conditions for Duhrssen's incisions of the cervix and forceps delivery are not favorable. Too long a delay in the performance of a cesarian section when parturients failed to be benefited by intravenous administration of oxytocin injection was a contributory factor in the neonatal deaths of two infants.

Carefully taken cultures reveal that the bacteria causing puerperal or postoperative sepsis seldom belong to a single species of micro-organism. Frequently, pathogenic bacteria are found as mixed groups, possibly consisting of gram-negative bacilli of the intestinal group or gram-positive cocci and bacilli. To counteract these bacteria more than one antibacterial agent should be employed. Penicillin, the safest and most dependable antibiotic, is weak in counteracting the effects of the gram-negative intestinal group bacilli; therefore, it should be supplemented by sulfadiazine or streptomycin to increase the chances of recovery. The use of two or more antibacterial drugs gives the patient the protection of their overlapping bacterial spectra, and these drugs act synergistically on the bacteria.[15] However, there is evidence that certain antibiotics may even show antagonism. Chloramphenicol, for example, may interfere with the action of penicillin.[16] Antibiotics must therefore be selected carefully.

Single long acting large doses of penicillin may be sufficient in the absence of intrapartum fever; however, with sepsis already present, antibacterial drugs should be used in large doses, frequently repeated throughout the 24 hours of each day. In all cases the administration of antibacterial medications should continue postoperatively until the mother is afebrile for three full days. If a cesarian section is deemed necessary for a patient who has not

11. McKelvey, J. L.: Cesarean Section, J. Iowa M. Soc. **32**: 281 (July) 1942.

12. Neglected cases were considered to be those of prolonged labors managed by private physicians or midwives in the home, usually for more than 24 hours, with no record of rectal or vaginal examination except the word of the patient, and cases in which attempts at delivery had failed.

13. Potential infection was considered to be present when labor had lasted more than 24 hours and/or membranes had been ruptured more than 12 hours, and actual infection was considered to be present when, in addition to a defined, potential infection, there were clinical manifestations of sepsis, such as intrapartum fever, chill, and purulent and foul amniotic fluid.

14. When oxytocin injection is given hypodermically, one should start with a dose of 0.5 minims (0.03 cc.), increasing the dose by 0.5 minims every 20 minutes, until a maximum dose of 2.0 minims (0.12 cc.) is reached, or until the uterine contractions resemble those that are normal in the first stage of active labor. When given intravenously, 10 minims of oxytocin injection should be diluted in 1 liter of 5% dextrose solution and administered at a rate of 1 drop every 2 seconds, or 50 to 60 cc. per minute. During the administration of oxytocin injection (hypodermically or intravenously), the patient must be constantly observed in order to check frequently the fetal heart rate and the character and frequency of uterine contraction.

15. Lyons, C.: Antibacterial Therapy in Gynecologic Surgery and Pelvic Infections, in Meigs, J. V., and Sturgis, S. H., editors: Progress in Gynecology, New York, Grune & Stratton, Inc., 1950, vol. 2, chap. 10, pp. 724-738.

16. Jawetz, E.; Gunnison, J. B.; Speck, R. S., and Coleman, V. R.: Studies on Antibiotic Synergism and Antagonism: The Interference of Chloramphenicol with the Action of Penicillin, A. M. A. Arch. Int. Med. **87**: 349 (March) 1951.

received the above recommended treatment the preoperative management should be revised. Chemotherapy should be instituted at once. A patient so neglected needs time to bolster her resistance. The only exception to this would be signs of a threatened rupture of the uterus. Fluids should be administered intravenously while the patient is being rested by sedation. During this period the patient should receive large doses of antibacterial agents in combinations that will fortify her against the bacteria that usually cause puerperal infection. By treating the patient in this manner while the operation is temporarily deferred, a smoother postoperative convalescence and less febrile morbidity are achieved. Transfusions of whole blood are invariably given to infected patients prior to abdominal delivery.

ANALYSIS OF FORTY TRANSPERITONEAL CESARIAN SECTIONS

In the interval since our last report [10] a period of 16 months has elapsed, and we have added a second series of 40 cases. Twenty-four of the patients originated from our services at the Cook County Hospital and 16 from private hospital practice and consultations. Thirty-four

Two Series of Potentially and Actually Infected Parturients Who Had Transperitoneal Cesarian Sections

	1st Series	2nd Series	Total
Number of patients	100	40	140
Incidence of morbidity *	45 (45%)	9 (22.5%)	54 (38.6%)
Actually infected patients	47	18	65
Morbidity	27 (57.4%)	5 (27.7%)	32 (49.2%)
Potentially infected patients	53	22	75
Morbidity	18 (33.9%)	4 (18.2%)	22 (29.3%)
Failed forceps	5	3	8
Maternal deaths	0	0	0
Fetal deaths	5 (5%)	4 (10%)	9 (6.4%)
Bladder injuries	0	1 †	1
Peritonitis	0	0	0

* Febrile postoperative morbidity.
† Classical cesarian section.

(35%) had labors characterized by dysfunctional uterine action or inertia. The longest labor was 97 hours, and the longest interval between rupture of membranes and delivery was 107 hours. Nine patients had one or more previous childbirths. In two of these patients the previous parturition was also dystocial. The most frequent indication, singly or in association with other conditions, is dysfunctional uterine action (inertia). It was the only basis for a cesarian section in 19 cases; however, it occurred in association with brow presentation in 2 cases, with breech presentation in 5, with constriction ring in 3, and with cervical fibroid in 1. In 10 patients, borderline disproportions were the basic indication, but only 4 of this group had dysfunctional labor. Constriction ring was noted in five patients, but it was regarded as the basic reason for the cesarian section in only three. In the table a summary of data in this series of cases is compared to that in the past reported study. Eighteen patients were deemed actually infected and had intrapartum temperature elevations that ranged from 100 F (oral) to 104.2 F (rectal). Five patients had foul and purulent amniotic fluid. Twenty-two patients were considered potentially infected, having labors and/or ruptured membranes of more than 24 and 12 hours respectively. In this group there were three cases in which forceps delivery failed. With two exceptions, the convalescence of all mothers under this regimen was surprisingly mild. Only nine patients had morbidity. The longest period of morbidity was six days. This was in a patient who had adynamic ileus that lasted three days. One patient had a wound dehiscence necessitating resuturing and a long hospital stay of 36 days.

The morbidity in the current series of 40 cases is 22.5%, as compared to 45% in the previous report. The table, which compares the two series, indicates that we now have had 140 cases without any mortality and that there is a definite tendency toward a decreased postoperative febrile morbidity. In the first report, with no precedent to guide us, we had to learn by trial and error. It is now definitely believed that it is not the type of cesarian procedure that minimizes the postoperative sepsis hazard but rather the medical management that bolsters the patient's resistance, particularly chemotherapy. While we prefer the lower uterine segment procedure, the following interesting case can be cited to demonstrate the gratifying effects of antibiotics in a grossly infected patient who had a classical cesarian section.

L. L., a Negro primigravida, 34, had an intrapartum temperature of 101.4 F. The membranes ruptured one hour before the onset of labor. The labor was dysfunctional and could not be altered favorably by intravenous oxytocin injection administration. Penicillin was administered eight hours prior to the performance of a cesarian section. The amniotic fluid became purulent and had a foul odor. A cesarian section was scheduled after 31½ hours of labor. The bladder, catheterized preoperatively, was at a high level and was inadvertently opened. After this was sutured, it was deemed wiser to perform a classical cesarian section. The patient received whole blood on two occasions, and penicillin and streptomycin were given in large doses. She was out of bed on the 3rd postoperative day, had no febrile morbidity, and left the hospital with a normal baby on the 11th day. Examination of the afterbirth revealed a moderate degree of placentitis.

SUMMARY AND CONCLUSIONS

A low cervical cesarian section, when indicated, equals any other procedure in assuring the patient's recovery when potential or actual infection is present. We believe the absence of postoperative septic mortality was due to the medical management and not to the particular cesarian section procedure used. Although antibacterial therapy, prophylactic or otherwise, is most important, previously established adjuncts of management must be utilized. Two or more antibacterial drugs were used with good effect. The administration and dosage of penicillin varies with the presence of potential or actual infection.

These conclusions are the result of a study of 140 consecutive parturients who were potentially or actually infected. The absence of any maternal mortality and a satisfactory postoperative recovery lead to the conclusion that this type of management yields the best results.

25 E. Washington (Dr. Kobak).

Psychotherapy in General Practice.—There are many levels of psychotherapy, most of which the general practitioner can work at with assurance. We might use three large categories for illustration: (1) diminution of external pressures by rearranging the life situation when possible; (2) support by reassurance, ventilation, suggestion, discussion, re-evaluation, and re-education; (3) more thorough examination of those personality conflicts in which the causes are not known to the patient. Only this latter group may require the help of a psychiatrist if they do not benefit from other measures. Henry W. Brosin, M.D., Psychotherapy for the General Practitioner, *The Pennsylvania Medical Journal*, January, 1952.

IMPORTANCE OF EARLY DIAGNOSIS IN ACUTE RHEUMATIC FEVER

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The fundamental cause of rheumatic fever remains obscure; nevertheless, progress is being made in conquering this disease, a leading killer of school age children and a leading cause of cardiac crippling in youth and young adults. The significant observation [1] that active rheumatic involvement may be "nipped in the bud" by the early administration of corticotropin (ACTH) or cortisone places even greater responsibility on the practicing physician. Practically all children acutely ill with rheumatic fever are first seen in the home or the office; hence the path is clear—every physician who sees children in his everyday practice must be thoroughly familiar with all clinical aspects of acute rheumatic fever and must be constantly on the alert for its occurrence.

MANIFESTATIONS

The first objective is to become increasingly familiar with the early manifestations of the disorder. Few diseases approach rheumatic fever with respect to variety as well as variability in intensity of the signs and symptoms. The peak age of onset is about 6 to 8 years; however, onset may occur throughout school age (5 to 15 years). I have made an attempt, on the basis of data previously collected,[2] to list the manifestations of rheumatic fever and estimate their approximate incidence at the onset and during and after the course of the disease (table 1), i. e., the acute and subacute activity, periods of likelihood of recurrences, and residual cardiac damage.

Pain is a particularly significant manifestation. Although typically it is present in the region of the joints, it may occur in the abdomen, chest, and various muscle groups. When joint pain is associated with swelling, redness, and tenderness, as in migratory polyarthritis, the disease is readily recognized. About one-fourth of the attacks have this type of manifestation initially, whereas about two-thirds of patients at some time or other will have polyarthritis. Mild arthritis or myositis, or even tenosynovitis, occurs with about the same frequency, although the symptoms may be so mild as to escape early detection by the parents. When the mild or vague pains occur in the region of the joints, especially those of the upper extremity, they are apt to be of rheumatic origin. The rheumatic pain is present often on awakening in the morning and frequently causes the child to limp but tends to disappear in the evening, when the child is in bed. The nonrheumatic pains associated with fatigue or postural derangements may be confusing. Fatigue pains are commoner in somewhat younger children, are more pronounced after the child retires, and are improved usually when the involved region is massaged. Some of the so-called growing pains may be of rheumatic origin. Abdominal pain occurs frequently in children with rheumatic fever and, when not associated with pain in the extremities or other findings suggestive of the disease, may be difficult to evaluate. At some time or other, about one-eighth of the children with acute rheumatic fever have abdominal pain as the outstanding complaint. When pain in the region of the thorax is the chief complaint, it is usual to find other evidences of rheumatic fever. A general rule might be that, whenever a child of school age complains of pain, serious thought should be given to the possibility of a rheumatic infection as being causative.

Rheumatic carditis is extremely variable with respect to incidence and severity of early manifestations. If one suspects the possibility of rheumatic fever, careful attention must be given to the examination of the heart. Significant features are development of murmurs, systolic or diastolic; alterations in rhythm, such as tic-tac and gallop rhythms; changes in the magnitude of heart tones; development of friction rubs; and shifts in the size and configuration of the heart. When there is no evidence of congenital heart disease or renal disease, the development of signs of cardiac decompensation in the child must be considered as of rheumatic origin until proved otherwise. It is estimated that about 10% of children with rheumatic fever have a cardiac murmur without other evidences of the disease.

Whether chorea minor is exclusively a manifestation of rheumatic fever is not known.[3] The incidence of residual heart disease is less in patients whose illness is compatible with Sydenham's chorea without other evidences of rheumatic fever than in those who likewise

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1. Hench, P. S., and others: The Effects of Adrenal Cortical Hormone 17-Hydroxy-11-Dehydrocorticosterone (Compound E) on the Acute Phase of Rheumatic Fever: Preliminary Report, Proc. Staff Meet., Mayo Clin. **24**: 277-297, 1949. Massell, B. F., and others: The Clinical Response of Rheumatic Fever and Acute Carditis to ACTH, New England J. Med. **242**: 641-647 and 692-698, 1950. Hench, P. S.; Slocumb, C. H.; Polley, H. F., and Kendall, E. C.: Effect of Cortisone and Pituitary Adrenocorticotropic Hormone (ACTH) on Rheumatic Diseases, J. A. M. A. **144**: 1327-1335 (Dec. 16) 1950. Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: Effects of Cortisone Acetate and Pituitary ACTH on Rheumatoid Arthritis, Rheumatic Fever and Certain Other Conditions: A Study in Clinical Physiology, Arch. Int. Med. **85**: 545-666, 1950. Wilson, M. G., and Helper, H. N.: Effect of Pituitary Adrenocorticotropic Hormone (ACTH) in Acute Rheumatic Carditis, J. A. M. A. **145**: 133-138 (Jan. 20) 1951. Dorfman, A.; Bergenstal, D. M.; Benditt, E. P., and Moses, F. E.: Effect of Pituitary Adrenocorticotropic Hormone (ACTH) on Rheumatic Fever, Proc Am. Ped. Soc. (May 9-10) 1950, A. M. A. Am. J. Dis. Child. **80**: 885-886, (Nov.) 1950. Barnes, A. R.: Effects of Cortisone and ACTH in 14 Patients with Acute Rheumatic Fever, Proc. Staff Meet., Mayo Clin. **25**: 478-479, 1950. Massell, B. F., and Warren, J. E.: Effect of Pituitary Adrenocorticotropic Hormone (ACTH) on Rheumatic Fever and Rheumatic Carditis, J. A. M. A. **144**:1335-1341 (Dec. 16) 1950. Harris, T. N.; Abrams, W. B.; Leo, T. F. P., and Hubbard, J. P.: Preliminary Observations on the Effects of Cortisone in the Treatment of Acute Rheumatic Carditis, Proc. Am. Ped. Soc. (May 9-10) 1950, Am. J. Dis. Child. **80**: 884-885, 1950. McEwen, C., and others: The Effect of Cortisone and ACTH on Rheumatic Fever, Bull. New York Acad. Med. **26**: 212-228, 1950.

2. Hansen, A. E.: Rheumatic Fever: Acute Rheumatic Fever and Acute Rheumatic Heart Disease, in Meyers, J. Arthur, and McKinlay, C. A., editors: The Chest and the Heart, Springfield, Ill., Charles C Thomas, Publisher, 1948, sec. 2, pp. 1543-1578.

3. Kagan, B. M., and Mirman, B.: Sydenham's Chorea: A Syndrome for Differential Diagnosis, J. Pediat. **31**: 322-332, 1947. Kagan, B. M.; Rosner, D. C., and Rosenblum, P.: Chorea (Sydenham): A Study of 58 Additional Patients, Am. J. Dis. Child. **78**: 306-313, 1949. Timme, A. R.: The Choreiform Syndrome: Its Significance in Children's Behavior Problems, California Med. **68**: 154-158, 1948.

have other manifestations of the disease. Nevertheless, from a practical viewpoint, the school age child who has the typical dystonia, muscle weakness, and emotional change should be considered as having rheumatic disease until proved otherwise.

Subcutaneous fibroid nodules are said to be found in about 15% to 20% of patients with rheumatic fever at some time or other over a period of years. The presence of the nodules is important from several viewpoints: First, they are almost pathognomonic of the disease; second, they usually occur in severely involved patients; third, they tend to occur during the subsiding phase of an acute attack. The frequency with which they are discovered seems to vary directly with the intensity with which they are sought.

TABLE 1.—*Outstanding Signs and Symptoms with Approximate Incidence of Manifestation at Onset, During, and After the Course of Rheumatic Fever*

Manifestation	Incidence, %	
	At Onset	Later
Pain		
In extremities		
Polyarthritis	25	66
Mild arthritis or myositis	25	66
In abdomen	..	12
In chest	Few	(?)
Carditis	..	80
Murmurs with enlargement	Many	Many
Gallop rhythm	Few	(?)
Muffled tones or pericardial rubs	Few	(?)
Decompensation	Few	25
Murmurs alone	Many	10
Chorea minor	25	50
Subcutaneous fibroid nodules	2.5	20
Skin changes	2.5	12
Miscellaneous (nephritis, pyelitis)	1	5
Constitutional symptoms (anorexia, weight loss—or failure to gain—pallor, epistaxis, fatigability, upper respiratory infections, listlessness, fever, nervousness, swelling)	Many	90

Erythema rheumatica (annulare) is the most typical of the skin manifestations of the disease, but erythema nodosum, erythema multiforme, purpura, petechiae, and urticaria may occur.

Although patients with rheumatic fever occasionally have symptoms compatible with acute glomerulonephritis, the interrelationship between the two diseases has not been delineated. Occasionally iritis, orchitis, pleuritis, pneumonitis, encephalitis, and other bizarre types of involvement are believed to be manifestations of rheumatic fever.

The constitutional symptoms as indicated in table 1 are important manifestations of rheumatic infection, and in some children the evidences of the disease may be no more definite than might be attributed to many other disorders. In a recent study LeBus and Panos [4] found that 9 out of 10 of their patients with rheumatic fever had some one or combination of these symptoms. Epistaxis was a prominent symptom in 18% of 91 children studied by them.

4. LeBus, H., and Panos, T. C.: Study of 91 Children from Rheumatic Fever in the Gulf Coast Area of Texas, Texas Rep. Biol. & Med. **10**: 45-52 (Spring) 1952.

5. Hansen, A. E.: Conditions Causing Confusion in the Diagnosis of Rheumatic Fever in Children: Analysis of Diagnosis Made by Practicing Physicians in 271 Rheumatic Subjects, J. A. M. A. **121**: 987-991 (March 27) 1943.

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DIAGNOSIS

Thorough familiarity with the manifestations of acute rheumatic fever is essential, as an unequivocal diagnosis cannot be made on the basis of laboratory tests. True enough, one may obtain assistance in arriving at a diagnosis by evaluating the leukocyte and differential counts, erythrocyte sedimentation rate, Weltmann reaction, antistreptolysin titer, antihyaluronidase, mucoproteins, antifibrinolysins, blood culture, electrocardiographic tracings, roentgenographic studies, vital capacity, venous pressures, and biopsy. The final diagnosis, however, rests on the interpretation of the various clinical findings. The patient's failure to react favorably to administration of sulfonamides or antibiotics may be significant in directing one's thoughts to the possibility of rheumatic fever. Helpful in this regard is the knowledge of disorders likely to be confused with acute rheumatic fever.

DIFFERENTIAL DIAGNOSIS

Some time ago, I reviewed various textbooks and periodicals; there were mentioned about 60 different disorders to be considered in the diagnosis of rheumatic fever and rheumatic heart disease. A study [5] was made of the referring and admitting diagnoses for 271 children with rheumatic fever. Dr. Howard LeBus collected further data of this type, so that there are now available the records of 435 children who were admitted to the University of Minnesota Hospitals and the University of Texas Medical Branch Hospitals. The diagnosis of rheumatic fever had been made on admission in three-fourths of these children; however, it was apparent that in some the diagnosis should have been made earlier. The types of disorder that caused confusion in the remaining fourth of the children were as follows: appendicitis, 25%; "nervousness," 23%; fulminating infection, 21%; low grade infection, 14%; poliomyelitis, 8%; osteomyelitis, 5%; sickle cell disease, 2%, and rheumatoid arthritis, 2%. Another approach [6] to the problem of the differential diagnosis has been to study the diagnoses made for almost a thousand children admitted to the pediatric service during one year to ascertain which conditions involved symptoms suggestive of rheumatic fever. In table 2 are summarized the disorders found to be especially important as determined from the above two approaches.

TABLE 2.—*Disorders Important in the Differential Diagnosis of Rheumatic Fever in Relation to Types of Manifestations*

Pain and Fever		
Appendicitis	Rheumatoid arthritis	Leukemia
Poliomyelitis	Sickle cell disease	Hodgkin's disease
Osteomyelitis	Meningococcemia	Nephritis
Nervousness		
Emotional disorder	Hyperthyroidism	Malnutrition
Fulminating infection		
Sepsis	Bacterial endocarditis	Pneumonia
Low grade infection		
Sinusitis	Infected tonsils and adenoids	Brucellosis

In some diseases the "therapeutic test" serves a valuable purpose with respect to diagnosis. To some extent with reference to rheumatic fever, the effect of the administration of salicylates has been of diagnostic value to the clinician. The question arises as to whether the use of corticotropin or cortisone might constitute another "ther-

apeutic test" in the diagnosis of rheumatic fever. Adrenocortical hormone, directly or indirectly through the influence of the pituitary adrenocorticotropic hormone, exerts nonspecific influences on fever, pain, and general well-being. From this viewpoint it seems that the adrenocortical hormone would be of limited usefulness diagnostically. However, the reported spectacular recession of pain (also swelling and tenderness) in rheumatic polyarthritis, associated with loss of febrile reaction, fall in erythrocyte sedimentation rate, and particularly the decline in evidences of early carditis, indicates that possibly there has been brought to the fore a new type of diagnostic tool as well as a therapeutic agent. As encouraging as the new hormonal therapy has been in early rheumatic heart disease, its effectiveness in well-established rheumatic carditis has been disappointing.

In many medical centers throughout the world, studies are now being made that eventually will clarify the therapeutic role of adrenocortical hormone in rheumatic fever. Inasmuch as conditions vary in regard to important features of the disease from one part of the country to the other, some controversial conclusions may be expected. Until complete agreement is reached, what is to be the procedure for the physician seeing the child early in the illness at home, far removed from a medical center? Heretofore, it has been acceptable practice to pronounce the condition in a given case as "possible rheumatic fever and rheumatic heart disease," and at the same time to adhere to recognized procedures in management. In questionable cases the physician was allowed plenty of time to make his final decision regarding the diagnosis. In the event rheumatic fever was not responsible for the symptoms, it was possible to allay parental fears and thereby prevent the creation of emotional problems that may be derived from the prospect of the particular child's becoming a "cardiac cripple."

The suggested procedure is (1) careful consideration of the details of the history and physical examination and (2) laboratory studies, including routine blood cell counts, erythrocyte sedimentation rate, and special laboratory studies if available. Of course, these steps are the same as for any other diagnostic problem. If the evidence points to the possibility of early rheumatic fever, it seems that one may give a "therapeutic trial" with corticotropin. The dangers of overdosage with adrenocortical hormone associated with prolonged administration are well known (full moon facies, acne, striae, lethargy, hirsutism, depletion of body potassium, sodium retention with water accumulation, and decreased resistance to infection). Because of the possible harmful effects, it is felt that the initial trial should be with minimal dosage for the shortest duration possible. At the present time it appears that 0.010 or 0.015 gm. of corticotropin given every six hours intramuscularly for four to six days, and possibly up to 10 days, should serve the purpose and still be safe for the average child. If evidence of early carditis is definite, one may give twice this amount for the first three days. Although the dosage is somewhat higher, cortisone has the advantage that it may be given orally. The child should be at complete bed rest. Temperature, pulse, respiration, blood pressure, and body weight should be studied in conjunction with critical examination of the patient with particular reference to the heart. If at all possible, daily total eosinophil counts should be used for determination of therapeutic range of effectiveness. If the evidence of improvement is not clear-cut after such a trial period, every attempt should be made to have the child hospitalized for more detailed study. In the event a favorable effect seems to have been obtained, with subsidence of pain and fever, decreasing sedimentation rate, and disappearance of cardiac murmurs, then the follow-up care should be the same as for any other child afflicted with acute rheumatic fever.

COURSE OF DISEASE

Of major importance in caring for the child with rheumatic fever is the evaluation of the status of activity of infection. Again, this is accomplished on the clinical basis by consideration of history, physical examination, and the results of laboratory studies. If we bear in mind the possibilities of the duration of an attack on the basis of past experiences, at least we may avoid one of the greatest dangers, namely, too early release of the patient from critical observation. Data from McCue and Galvin [7] have

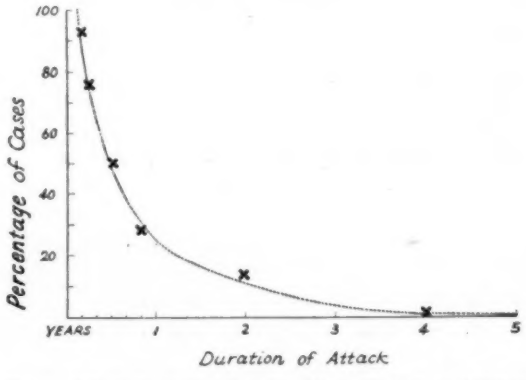

Fig. 1.—Schematic representation of the variability in duration of early (first and second) attacks of rheumatic fever (McCue and Galvin [7]).

been summarized and presented schematically (fig. 1) to show the extreme variability in an attack of rheumatic fever. In about one-third of the patients, the duration was less than four months. In about 20%, the duration was over one year with a small proportion having rheumatic activity three to five years. A rather extensive experience will be required for evaluation of the effect of the administration of corticotropin on the average duration of an attack as well as the consequent degree of cardiac damage.

Experience with three children is summarized in figures 2, 3, and 4 by my colleague Dr. R. W. Carabelle, to illustrate some of the features of the effect of corticotropin therapy in rheumatic fever.

A favorable effect was obtained in case 1 as indicated by cessation of joint pain, decrease in total white cell count, sharp decline in the erythrocyte sedimentation rate, and decrease in the area of the cardiac silhouette. No significant alteration was noted in the systolic murmur at the apex. In case 2 there was rapid disappearance of pain but no decided changes in the laboratory findings. The least one can say is that during this time interval the

7. McCue, C. M., and Galvin, L. F.: A Preliminary Report on Rheumatic Fever in Virginia, J. Pediat. 33: 467-483, 1948.

cardiac status was not aggravated. In case 3, although there was some symptomatic improvement with respect to pain, fever, and evidences of heart failure, the other clinical and laboratory findings remained unaltered. This child had a severely damaged heart as a result of his first attack one year previously.

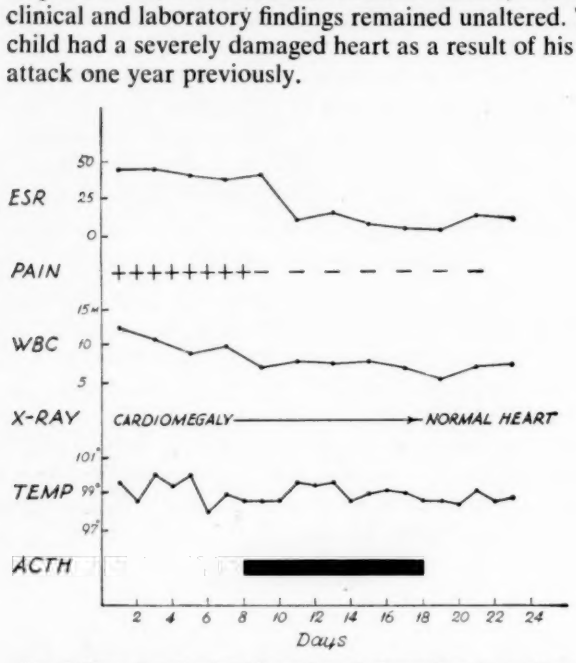

Fig. 2 (Case 1).—Graphic illustration of observations in an 11-year-old boy who had his initial attack of rheumatic fever with onset of polyarthritis and fever six weeks before admission. He was given 0.06 gm. of corticotropin daily in four divided doses for a period of 10 days. (ESR, erythrocyte sedimentation rate.)

MANAGEMENT

Administration of corticotropin or cortisone does not seem to alter the over-all treatment of children with rheumatic fever. The intake of potassium should be adequate

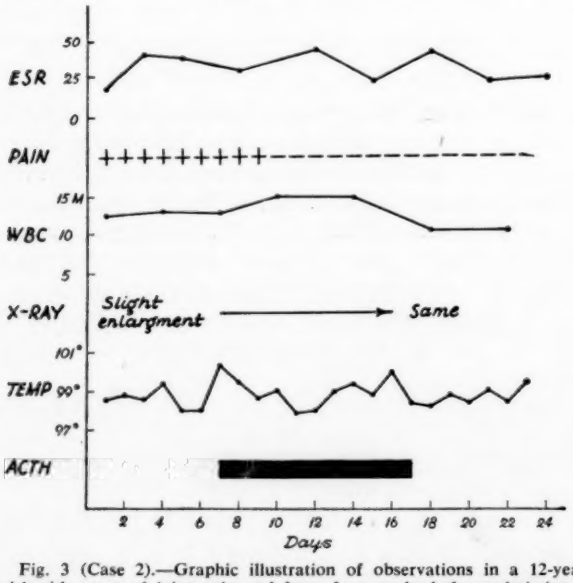

Fig. 3 (Case 2).—Graphic illustration of observations in a 12-year-old girl with onset of joint pain and fever four weeks before admission. She was given 0.06 gm. of corticotropin daily in four divided doses for a period of 10 days. When she was almost 4 years of age, the child had joint pains and the parents were informed by the family physician that she had a heart murmur.

and excessive amounts of sodium chloride avoided. The following outline includes the major points in management of the patient who is kept under the care of the family physician.

ACUTE PHASE—SYMPTOMATIC

Pain and Fever: bed rest, salicylates (0.10 to 0.15 gm. per kilogram of body weight), e. g., aspirin; nutritious diet; oxygen, especially with carditis; and comfort and security.

Chorea Minor: bed rest, quiet environment, protection from injury, nutritious diet, and sedation (phenobarbital sodium is satisfactory usually).

Decompensation: strict bed rest, oxygen, sedation, low sodium diet, diuretics, and digitalis.

SUBSIDING PHASE—GRADUATED PHYSICAL EXERCISE

Nutritious diet with iron and vitamin supplements, diversional therapy, physical therapy, educational program, positive program for increasing physical activity, psychological conditioning to prevent overanxiety, and removal of foci of infection (use of sulfonamides or penicillin during such times).

QUIESCENT PHASE—PREVENTION OF RECURRENCES

Sulfonamide, penicillin or other antibiotics, nutritious diet, periodic examinations.

From experiences with corticotropin in the treatment of rheumatic infection, there is every reason to believe that children so treated are likely to experience recurrent

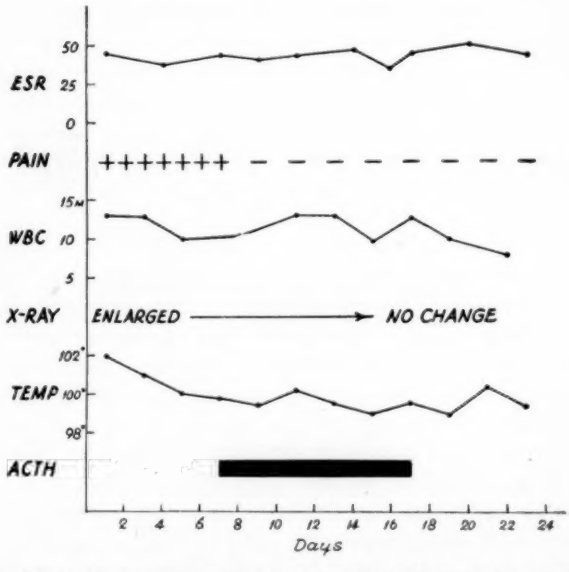

Fig. 4 (Case 3).—Graphic illustration of observations in a 9-year-old boy with onset of severe migratory polyarthritis, fever, and dyspnea seven days prior to admission. He was given 0.06 gm. of corticotropin daily in four divided doses for 10 days. He had had his initial attack of rheumatic fever about one year previously.

attacks. Only 20% to 30% of children afflicted with rheumatic fever have but a single attack. Although two or three attacks are usual, some patients apparently will have up to 10 or more different rheumatic episodes. The younger the child is at the time of the first attack, the longer is the period he or she is likely to have a recurrence. The interval between attacks may be weeks or years, 67% of subsequent attacks occurring within three years and 80% within five years of an attack.

In some parts of the country the problem of rheumatic heart disease has been made a community responsibility, with extensive programs in well-equipped hospitals and convalescent homes. In many of the states, the child handicapped with heart disease is eligible for assistance under the various state crippled children's programs. In many convalescent homes and under organized programs of various types, the problem of prevention of recrudescences has been well worked out. Administration of peni-

cillin during the acute phase of beta hemolytic streptococcic infections, and also in the carrier state, has proved to be effective.[8] All too few practicing physicians have facilities for bacteriological study; hence the use of penicillin in this way has its limitations in actual practice. The effectiveness of continuous administration of penicillin [9] or of other antibiotic agents, though encouraging, has not been evaluated adequately to warrant recommendation. An incidental factor to consider is that of expense. On the other hand, a considerable experience with the use of sulfonamides has been gained during the past 15 years. In a summary [2] of the work of several groups, it was found that, with daily sulfonamide administration for 885 patient-years, there were 18 recurrent attacks. In 723 patient-years of observation with control subjects, not receiving sulfonamides, there were 140 recrudescences. In most of the earlier studies sulfanilamide was employed, but, in recent years, sulfadiazine seems to have become the drug of choice.[10] For children up to 10 years of age, 0.25 gm. is given with the morning and evening meals; for children over this age the dose is 0.5 gm. Jackson and co-workers [11] have emphasized the importance of an adequate diet in the prevention of recurrences.

CONCLUSION

The physician plays a particular role in the problem of rheumatic fever in childhood by emphasizing the importance of adequate follow-up for the child with rheumatic fever. For all patients, including those who have been given corticotropin (ACTH) or cortisone for the treatment of early rheumatic fever, a prophylactic regimen should be instituted as soon as there are evidences that the activity of the infection has subsided. Recurrences may then be greatly lessened, the incidence of bed-confining illness may be diminished, and the number of "cardiac cripples" may thus be reduced. From a consideration of the various phases of the rheumatic fever problem, one point is indisputable: the drive of medical science to discover the fundamental cause and cure of rheumatic fever must continue in order to conquer one of the most important problems of the childhood period.

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9. Brick, M., and others: Oral Penicillin Prophylaxis in Rheumatic Fever Patients, Canad. M. A. J. **63**: 255-258, 1950. Maliner, M. M.: Oral Penicillin in the Prophylaxis of Recurrent Rheumatic Fever, J. Pediat. **37**: 858-861, 1950. Hofer, J. W.: Oral Penicillin for Children with Rheumatic Fever, ibid. **35**: 135-144, 1949.

10. Baldwin, J. S.: Sulfadiazine Prophylaxis in Children and Adolescents with Inactive Rheumatic Fever, J. Pediat. **30**: 284-288, 1947.

11. Jackson, R. L.; Kelly, H. G.; Rohret, C. H., and Duane, J. M.: Rheumatic Fever Recurrences in Children Without Sulfonamide Prophylaxis: An Evaluation of Environmental Factors, J. Pediat. **31**: 390-402, 1947.

CLINICAL EXPERIENCE WITH STREPTOKINASE AND STREPTODORNASE IN TUBERCULOSIS

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Streptokinase and streptodornase are useful topical adjuncts in the surgical treatment of certain acute and chronic diseases. The properties of these compounds and the results of treatment have been reported in detail elsewhere.[1] Streptokinase is a catalytic agent acting on a fibrin-lysing system present in the euglobulin fraction of human blood. The agent activates the fibrin-lysing system, which causes liquefaction of fibrin. Streptokinase also inhibits the change of fibrinogen to fibrin. Tests of streptokinase for protein give positive results. The substance is rendered inert by trypsin and activated papain, does not act upon casein, peptone, or gelatin, and can be isolated from the dissolved fibrin clot after completion of liquefaction. Streptokinase is antigenic, and an antikinase may develop in human beings as the result of antecedent hemolytic streptococcic infection or prolonged treatment with streptokinase. Streptodornase is an enzyme having the capacity to hydrolyze desoxyribose nucleoprotein. Kunitz [2] has described the properties of streptodornase, which he called desoxyribonuclease. Streptodornase is well preserved if stored at about 4 C and has a specific action. In highly diluted solutions, the enzyme has little action. The optimum pH for activity ranges from 6.8 to 8.2. Heat inactivates the enzyme rapidly, and exposure to a temperature of 55 C for 15 minutes destroys more than 90% of the substance. The enzyme system requires catalytic activation by the magnesium or manganese ion. To maintain activity, the ampules containing the desiccated mixture of streptokinase and streptodornase should be stored at a temperature of about 4 C. The material may be used in solution or as an ointment but must be stored properly. The contents of an ampule are readily soluble in 20 cc. of sterile isotonic sodium chloride solution. Vigorous shaking should be avoided. When prepared, the solution should be used immediately or it will lose its potency on standing at room temperature, especially in relation to streptodornase. When divided doses of an ampule are administered, the remainder is placed in a sterile container, fast-frozen, and stored in a deep freeze

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until needed for therapy. In the process of thawing such tubes, heating above 35 C should be avoided. When used as an ointment, 100,000 units of streptokinase and 60,000 units of streptodornase are incorporated in 10 cc. of lubafax,® a water-soluble base. The addition of antibiotics to this suspension may prove useful to control surface infection. We have used 250 mg. of soluble crystalline aureomycin. The advantages of the use of such a mixture is readily appreciated in the treatment of superficial infections or burns.

It must be emphasized that the enzymes do only two things when they are placed in proximity to the area of infection. Streptokinase causes the liquefaction of fibrin, and streptodornase causes the hydrolysis of desoxyribose nucleoprotein and desoxyribose nucleic acid. The healing of infected wounds is enhanced by the removal of these substances, but the use of the enzymes does not completely eliminate the need for the application of the usual therapeutic surgical procedures. Streptokinase and streptodornase are only surface acting compounds producing a selective chemical débridement of the infected wound. Since they are surface acting compounds, the best results have been obtained in cases in which complete exteriorization of the infected area has been possible. If this is not possible owing to anatomic location, the means for drainage should be as adequate as possible. Adequate circulation to the local area is necessary, since the fibrin-lysing system of the blood must be carried to the affected area, for streptokinase does not have the ability to lyse fibrin by itself. Likewise, streptodornase must be activated by magnesium or manganese ion, which comes from the blood stream. When necessary, the blood supply to the affected part may be improved by heat, by elevation to decrease edema, by blocking the regional portion of the sympathetic nervous system with procaine, or by sympathectomy.

Necrotic tissue, which prevents satisfactory contact of the enzymes with the constituents of the wounds to be hydrolyzed, must be removed. Sloughing tissue, in addition, may contain trypsin, which inactivates streptokinase. Slough is an excellent culture medium for bacteria. Further, this dead tissue prevents proper contact of concurrently given chemotherapeutic or antibiotic agents with bacteria that may be buried in the slough. Normal reparative processes are inhibited by loculated collections of purulent material. Living leukocytes will not function in a pool of pus, since effective phagocytosis is obtained only when the leukocytes are in an ameboid state. The phagocytic activity of the leukocytes will be considerably enhanced by the removal of desoxyribose nucleic acid, a constituent of pus, which clumps leukocytes and prevents effective action. In like manner, the removal of fibrin permits better action of the leukocytes. The frequency of treatment will be conditioned by the severity of the infection and the response to therapy. Badly infected lesions may be treated every four hours, while in less severe cases only one application of the enzymes daily may be required.

Toxic effects from application to external wounds have as yet not been seen. Minor headaches and aching have been seen more frequently in the instances in which closed spaces were treated. When put into a closed space, such as the pleural cavity or knee joint, streptokinase and streptodornase usually will produce an elevation of temperature that occasionally may be moderately high. The products of digestion are probably one cause for the elevation of temperature; a second factor is the direct result of the cleansing produced by these compounds. The lysis of fibrin and desoxyribose nucleoprotein from the walls of a closed space may release bacteria that have been imprisoned, for it is not uncommon to obtain positive cultures after several days of treatment when previous cultures have been sterile. Prothrombin times determined in persons treated with streptokinase and streptodornase did not show significant alteration from the normal. Hematomas and areas of ecchymosis were not seen. Bleeding was not produced by the topical application of these compounds. Success did not always follow the use of streptokinase and streptodornase, but the results of treatment were uniformly good. A careful estimate of the situation must be made when effective action of the compounds is not obtained, because it is possible that some important obstacle to wound healing has been overlooked. The results in the treatment of pyogenic infections of the soft tissues were excellent. Those obtained in pyogenic osteomyelitis were encouraging, but sufficient time has not elapsed to permit a final analysis. Also, the results obtained in the treatment of extrapulmonary tuberculosis have been encouraging.

REPORT OF CASES

CASE 1.—A 26-year-old Negro was admitted to the orthopedic service of the Veterans Administration Hospital on May 5, 1948, for a tuberculous spondylitis of the second and third lumbar vertebrae. A spinal fusion was performed, and the patient was discharged on Jan. 26, 1949. He was seen at irregular intervals and finally admitted to the surgical service with a psoas abscess of the right side on May 20, 1949. Incision and drainage, with release of about 300 cc. of purulent material,

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2. Kunitz, M.: Crystalline Desoxyribonuclease: Isolation and General Properties: Spectrophotometric Method for the Measurement of Desoxyribonuclease Activity, J. Gen. Physiol. **33**: 349-377 (March) 1950. Kunitz, M.: Crystalline Desoxyribonuclease: Digestion of Thymus Nucleic Acid (Desoxyribonucleic Acid): The Kinetics of the Reaction, ibid. **33**: 363-377 (March) 1950.

were done on July 25. Tubercle bacilli were isolated from this pus after inoculation of it into a guinea pig. Streptomycin, 0.5 gm., was given intramuscularly twice a day from July 25 through Nov. 30 and from March 10, 1950, through June 1. Fifty thousand units of aqueous crystalline penicillin G was given intramuscularly every three hours from Aug. 4, 1949, through Aug. 17 and from Oct. 1 through Oct. 15. Three hundred thousand units of crystalline procaine penicillin G in oil was given intramuscularly once a day from Oct. 16 through Nov. 10. Aqueous crystalline penicillin G, 50,000 units, was given intramuscularly every three hours from Dec. 18 through Dec. 22 and March 10, 1950, through April 6. One hundred thousand units of aqueous crystalline penicillin G was given intramuscularly every three hours from May 12 through May 31. Another spinal fusion was done on Aug. 4, 1949, after which the patient was returned to the general surgical service for secondary closure of the wound created for drainage of the psoas abscess. After this procedure was done, a small sinus tract persisted. A left psoas abscess, from which tubercle bacilli were eventually isolated, began to develop. Incision and drainage of this abscess was done on March 10, 1950. Streptokinase, 45,000 units, and 15,750 units of streptodornase were put into the abscess cavity on March 13. Two further courses of streptokinase, 135,000 units, and streptodornase, 47,250 units, were given on March 16 and 19. Cultures for other bacteria were sterile on March 22. The wound was closed secondarily on March 23, about two weeks after the initial incision. Healing of this wound was complete on April 9. The sinus on the right side, which had not been treated with streptokinase and streptodornase during this period, had not changed in appearance or character. The treatment of this sinus, which had been present since July 7, 1949, was started on March 28. An average of 40,000 units of streptokinase and 19,000 units of streptodornase was placed in the sinus tract 18 times, at intervals of about two days, between March 28 and May 12, when the wound was closed secondarily. There was roentgenologic evidence that the sinus tract extended directly to the lumbar vertebrae at the site of the earlier spinal fusion. The persistence of the tract might be explained by this evidence. Healing was prompt, and the patient was discharged on June 2, 1950. A follow-up report on May 23, 1951, revealed that the patient had remained well.

Case 2.—A 52-year-old Negro was admitted to the Veterans Administration Hospital on March 9, 1949, with a left gluteal abscess of about three months' duration. Incision and drainage, with release of about 300 cc. of purulent material, was done on March 11. Culture and biopsy from the abscess showed tuberculosis. Fifty thousand units of aqueous crystalline penicillin G was given intramuscularly every three hours from March 11 through June 2. Streptomycin, 0.5 gm., was given intramuscularly twice a day from March 23 through May 7. The roentgenogram of the left hip showed a slight area of rarefaction in the greater trochanter, but further change had not occurred roentgenographically at the end of six weeks of observation. The tract became much smaller, and a secondary closure was done on May 26. A small draining sinus persisted until about the time of discharge, on June 27, 1949, but the wound healed finally. The patient was readmitted on Jan. 10, 1950, for treatment of a mass in the left supraclavicular region. Biopsy from this area showed chronic inflammation. This wound healed well. During the patient's stay in the hospital, a mass, which subsequently became fluctuant, developed in the left buttock at the site involved previously, upon the first admission. Incision and drainage of a large abscess was done on Feb. 20. Tubercle bacilli were isolated from the purulent material. Crystalline procaine penicillin G, 300,000 units in oil, was given intramuscularly twice a day from Jan. 24 through Feb. 6. Aqueous crystalline penicillin G, 100,000 units, was given intramuscularly every six hours from Feb. 20 through March 4. Sulfadiazine, 0.5 gm., was given orally four times a day from Jan. 24 through Feb. 6. Streptomycin, 0.5 gm., was given intramuscularly twice a day from Feb. 18 through April 10. Streptokinase, 90,000 units, and 30,500 units of streptodornase were applied topically to the wound three times between Feb. 23 and Feb. 28. The wound became healthy and clean. The roentgenogram of the greater trochanter now showed definite irregular mottled areas of radiolucency. The greater trochanter was removed through a separate incision on March 7. The wound was closed primarily, and healing was uneventful. A secondary closure of the wound, resulting from the incision and drainage of the abscess, was done on March 27. The wound healed without complication, and the patient was discharged on April 10.

Case 3.—A 24-year-old Negro was admitted to the Veterans Administration hospital on June 14, 1950, with a severe bilateral tuberculous lymphadenitis, which began in Sept., 1949. Subsequently, tuberculosis of the right knee developed. The patient was seen at another hospital and treated with streptomycin. Numerous small draining sinuses were present in the cervical area. The lymph nodes were markedly enlarged. The roentgenogram of the chest showed a minimal tuberculous lesion of the upper lobe of the right lung. Culture of the purulent material obtained from one of the cervical sinuses was sterile aerobically and anerobically for pyogenic bacteria but positive for Mycobacterium tuberculosis. Aqueous crystalline penicillin G, 50,000 units, was given intramuscularly every four hours from June 18 to June 21, when the dose was changed to 100,000 units every six hours and continued to July 18. Streptomycin, 0.5 gm., was given intramuscularly twice a day from June 19 to July 24. Streptokinase, 20,000 units, and 9,500 units of streptodornase were injected into the sinuses in the right side of the neck on June 18 and June 20. A dissection of the lymph nodes of the right side of the neck was done on June 23. During the dissection, a collection of about 10 cc. of purulent material was evacuated from an area posterior to the sternocleidomastoid muscle and extending behind the carotid sheath toward the midline of the neck. Drainage was provided through one of the posterior sinus tracts. The main wound was closed. Streptokinase, 50,000 units, and 23,750 units of streptodornase were inserted into the posterior drainage tract on June 28 and June 30. A resection of the lymph nodes in the left side of the neck was done on July 10. A Penrose drain was brought out of the lower end of the wound, which was otherwise closed. Healing of both wounds was uneventful. The patient was discharged from the hospital on July 26.

Case 4.—A 25-year-old Negro was admitted to the Veterans Administration hospital on Dec. 12, 1950, with a mass 2.5 cm. in diameter over the right seventh rib at the costochondral junction. Incision and drainage with evacuation of pus was done on Dec. 19. Biopsy at this time showed tuberculosis. Streptokinase, 25,000 units, and 15,000 units of streptodornase were applied topically to the wound daily from Dec. 21 through Jan. 1, 1951. Streptomycin, 0.5 gm., was given intramuscularly from Jan. 2 through March 8. Crystalline procaine penicillin G, 300,000 units in oil, was given intramuscularly once a day from Jan. 7 through Jan. 12, from Feb. 9 through Feb. 16, and from March 5 through March 8. Four grams of paraaminosalicylic acid was given orally three times a day from Jan. 18 through March 8. A secondary closure was done on Jan. 2, with healing by Jan. 15. The patient was transferred to the medical service for treatment of the pulmonary tuberculosis. The patient was again seen on April 26 for a mass about 2.5 cm. in diameter over the left seventh rib; this had been present for about one month. The wound on the right side was healed. Streptomycin, 1 gm., had been given intramuscularly twice a week, and 4 gm. of paraaminosalicylic acid had been given orally, starting on April 3, and was continued through the present period of treatment. An incision and drainage of the tuberculous abscess on the left side was done on May 8. Streptokinase, 18,750 units, and 6,250 units of streptodornase were applied topically to the wound on May 10 and May 11. The wound was healed by May 23 and did not require secondary closure. The patient was transferred to the medical service for further treatment of his pulmonary tuberculosis.

Case 5.—A 15-year-old Negro was admitted to the Baltimore City Hospital on Oct. 4, 1950, with tuberculosis of the vertebral column present for about 10 years. He was emaciated, underdeveloped, and paraplegic. A pronounced kyphosis and a sinus with copious purulent drainage were present over the midthoracic portion of the vertebral column. Roentgenograms showed destruction of the 4th, 5th, 8th, 9th, and 10th thoracic vertebras and the lower four right ribs. Streptomycin, 1 gm.,

was given intramuscularly every three days from Oct. 10 to Oct. 24. The amount was changed to 0.25 gm. every three hours from Oct. 24 to Oct. 29, when it was shifted to the original dosage. Paraaminosalicylic acid, 3 gm., was given orally three times a day, starting on Oct. 24, and is still being given. Aqueous crystalline penicillin G, 50,000 units, was given intramuscularly every three hours from Oct. 24 through Nov. 2. The four involved ribs were removed, and a large paravertebral abscess was drained on Oct. 23. The patient was put into a body cast. He improved considerably during the next few months and gained weight. The paraplegia became less severe. Drainage from the wound, which had an unhealthy look, with pale, edematous granulation tissue, persisted. It was felt that treatment with streptokinase and streptodornase might aid in obliterating the residual soft tissue cavity and that a fusion of the vertebral column might then be undertaken safely. Streptokinase, 50,000 units, and 25,000 units of streptodornase were inserted through a catheter into the wound twice a day, starting on Jan. 28, 1951. Digestion was allowed to proceed for four hours, and then air vent suction was provided to remove the products of disintegration until the time for the second instillation, when the cycle was repeated. Therapy was continued until Feb. 21, when the catheters were withdrawn. The wound responded well to treatment. The abscess cavity shrank from about 150 cc. to almost nothing. With healing of the wound and during treatment with enzymes, spinal fusion from the seventh thoracic through the first lumbar vertebra was done on Feb. 13. Further fusion was contemplated at a later date. The operative wound and the wound made to remove the ribs and drain the abscess healed. The paraplegia has disappeared. The patient is still in the hospital for further therapy.

CASE 6.—A 30-year-old Negress was admitted to the Baltimore City Hospital on March 7, 1951, for back pain of about eight years' duration but which had been more pronounced during the past six months. A tuberculous abscess was found in the right gluteal region. Incision and drainage was done on March 14. The right sacroiliac joint was determined to be the primary source of infection. The operative wound, which was closed without drainage, healed by primary intention. Streptomycin, 1 gm., and aqueous crystalline penicillin G, 300,000 units, were given intramuscularly twice a day from March 14 to April 2. Streptomycin, 1 gm., was given intramuscularly every three days from April 2 and is still being given. An extra-articular fusion of the right sacroiliac joint was done on March 29. The wound did not heal. Purulent material was noted in the wound on April 4 and was still present at the time therapy with streptokinase and streptodornase was started on April 24. The wound at this time was about 4 cm. in length and 4 cm. in depth, extending to the site of fusion. A polythene tube was placed into the wound and covered with a nylon pack. Streptokinase, 16,600 units, and streptodornase, 8,300 units, were injected into the tube every four hours until May 9, when the tube and pack were removed. The wound had decreased considerably in size and closed on May 21.

CASE 7.—A 17-year-old Negro was admitted to the Baltimore City Hospital on April 11, 1951, with a history of having a tuberculous cervical lymphadenitis for about one year. An incision and drainage of a tuberculous abscess had been done on June 7, 1950. An excision of a mass of tuberculous lymph nodes was done on July 7. A secondary closure and application of a split skin graft was done on Aug.14. The wound healed, and the patient did not have further difficulty until April 2, when a sinus just below the left angle of the mandible was noted. Streptomycin, 1 gm., was given every three days from April 13 to April 23, when the dose was increased to 1 gm. a day until May 11. Three grams of paraaminosalicylic acid was given orally three times a day from May 8 through May 13. The wound did not show any signs of healing with streptomycin and paraaminosalicylic acid treatment. An incision and drainage of the tract was done on April 23. A polythene tube was placed into the wound and was covered with a nylon pack. Streptokinase, 16,600 units, and streptodornase, 8,300 units, were injected through the catheter every four hours from April 24 through May 1. The wound improved considerably during this period. The catheter and pack were removed on May 1. A mixture of streptokinase and streptodornase in lubafax® with aureomycin was applied to the wound twice daily from May 2 through May 7. A secondary closure of the wound was done on May 8. A section of a small polythene tube was placed under the closure through a small stab wound. Streptokinase, 25,000 units, and 12,500 units of streptodornase were injected through the catheter twice a day on May 9 and May 10. The catheter was removed on May 11. Healing was by primary intention. The patient was discharged from the hospital on May 15.

COMMENT

The use of streptokinase and streptodornase will permit the surgeon greater security in the drainage of tuberculous abscesses. Although it would seem to us that such accumulations of pus delay healing, many surgeons are unwilling to drain such abscesses for reasonable fear of secondary infection and consequent deterioration of the patient. The results obtained so far indicate that such fear is not justified. The removal of thick purulent material from the walls of the cavity accomplished by the use of the enzymes will allow greater penetration and more effective action of antibiotics given either systemically or locally.

Since streptokinase and streptodornase are compounds having a surface action only, the best results are achieved when exteriorization is as complete as possible. The surface action of the compounds is a relative disadvantage in the treatment of infections of bone, where penetration of the dense matrix is poor. The use of the compounds is still indicated, but care must be exercised to place the compounds in the area of infection, and the duration of the treatment is longer. To date, 19 patients with tuberculous infections, of which 14 infections were severe, have been treated by these methods. These include 4 patients with tuberculous empyema, 5 patients with tuberculous lymphadenitis, and 10 patients with some manifestation of tuberculosis of the bones, joints, or tendons. In 16 of these, the tuberculous infection has been controlled, and all wounds and sinuses are healed. The remaining three persons had advanced, progressive tuberculosis. Local improvement was obtained in each of these, but the systemic progress of the tuberculosis continued with fatal result.

Care must be taken when streptokinase and streptodornase are used in the treatment of tuberculous empyema in the presence of a bronchopleural fistula. Thick pus in the empyema space is rapidly converted into thin material, which lends itself to ready aspiration or drainage. The enzymes, together with aspiration or drainage, will prepare the empyema cavity for successful subsequent thoracoplasty. The thick visceral pleura, which becomes well organized and relatively avascular, does not lend itself to chemical solution. Since thick pus in the empyema space is made thin by streptokinase and streptodornase, spread of the infection may easily occur in the presence of a bronchopleural fistula. This complication has not been seen in two instances, but enzymatic therapy in the presence of fistula must be undertaken with caution and followed as rapidly as possible by surgical collapse if an unyielding roof of bone is present. Experience with two instances demonstrated that fibrinous adhesions may be dissolved but that lysis of organized adhesions or adhesions containing collagen will not result from therapy.

SUMMARY

The rapidity of healing that is afforded by surgical drainage of tuberculous abscesses when it is combined with the use of streptokinase and streptodornase offers a more satisfactory way of treating these lesions than older conservative methods. Streptokinase and streptodornase must be used purely as adjuncts, however, to other therapeutic measures. The compounds have no effect upon living tissue and the use of these enzymes facilitates the formation of healthy granulation tissue. If spontaneous closure of wounds does not occur rapidly, secondary closure may then be carried out.

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TREATMENT OF ULCERATIVE COLITIS WITH CORTICOTROPIN (ACTH) AND CORTISONE

A TWO YEAR FOLLOW-UP

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The purpose of this communication is to report our experiences over a period of 2 years with the use of corticotropin (ACTH) and cortisone in a selected group of patients with ulcerative colitis. Studies were directed to determine the effectiveness of hormone therapy in inducing a remission in the disease. The possibility of sustaining the remission by long-term maintenance therapy and repeated courses of hormone treatment was investigated. Corticotropin therapy was begun in the first patient of this series (O. D.) on Oct. 2, 1949.

The use of corticotropin in ulcerative colitis is predicated on its effectiveness in reducing the extensive inflammatory tissue reaction that characterizes the disease and in diminishing the systemic and toxic manifestations of infection. Hormonal inhibition of fibroblastic proliferation with the possible prevention of fibrosis and stricture formation were additional indications. The dramatic increase in appetite and sense of well-being, which often characterize the administration of corticotropin and cortisone, might be anticipated to be of incalculable value in the treatment of these debilitated, anorexic malnourished patients.

Remissions have been induced by hormone therapy in a wide variety of systemic diseases involving mesenchymal tissue or in which an antigen-antibody type of reaction may be implicated. The occurrence of polyarthritis and the extensive mesenchymal involvement of the colon observed in this disease offered further incentive to this study.

Since the fecal lysozyme titer appears to reflect the activity of the ulcerative process,[1] the effect of hormone therapy on the fecal lysozyme level was integrated with the clinical course of the disease.

METHOD OF STUDY AND TREATMENT

The psychological effects of a new form of treatment were minimized whenever possible. The patients were given parenteral placebos in many instances before hormone therapy was begun and were not informed of the change in medication. A moderately unrestricted, bland diet was maintained unaltered through the control and treatment periods. All medication except the use of phenobarbital sodium was discontinued during the period of study.

In view of the spontaneous remissions that may occur in this disease, corticotropin and cortisone therapy was restricted to patients with severe intractable ulcerative colitis. Eight patients were selected who were almost completely incapacitated and had not responded to an adequate control period (one to four months) of good medical management, which included the use of antibiotics, detergents, prolonged bed rest, diet, and blood transfusions, with psychotherapy and the usual supportive treatment.

Six of the eight patients were acutely ill with intractable bloody diarrhea (8 to 15 evacuations daily), abdominal pain, tenesmus, anorexia, profound weight loss, fever, leukocytosis, and anemia. Two patients were chronically disabled by frequent uncontrollable, blood-tinged evacuations, moderate weight loss, abdominal distress, and anorexia. The sigmoidoscopic examination demonstrated a diffusely ulcerated, freely bleeding, friable mucosa, and the roentgen studies revealed extensive involvement of the colon and rectum.

Laboratory studies included determinations of the blood eosinophil count,[2] urinary 17-ketosteroids, as well as the sedimentation rate, serum proteins, fasting blood sugar, blood carbon dioxide, serum chlorides, hematocrit, hemoglobin, and white cell count.

The consistency, appearance, and number of stools were recorded daily, and the stools were analyzed for occult blood. The appearance of the colon was studied by repeated proctosigmoidoscopic and roentgen examinations. The fecal lysozyme titer [3] was determined at frequent intervals prior to, during, and after corticotropin therapy.

Objective criteria for remission consisted of control of diarrhea, decrease in fecal blood, fall in lysozyme titer, disappear-

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From the Medical Clinic, Peter Bent Brigham Hospital; the Department of Medicine and Biophysical Laboratory, Harvard Medical School; and the West Roxbury Veterans Administration Hospital.

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ance of fever, decrease in sedimentation rate, increase in body weight, and definite sigmoidoscopic evidence of healing.

Corticotropin was administered in doses of 20 to 40 mg. intramuscularly at six-hour intervals for periods of three to eight weeks, depending on the requirements and clinical response of each patient. At the end of treatment, the dose was reduced gradually over a period of five to seven days. Antibiotics such as penicillin, in doses of 300,000 to 400,000 units daily, were administered to some patients for four to five days during this period before the hormone therapy was discontinued. All patients were maintained on a limited salt and fluid intake and were given 0.9 gm. of potassium chloride three times daily. During the past year corticotropin was administered intravenously over an 8 hour period daily as a solution containing 20 mg. in 500 cc. of dextrose in water.

Cortisone was administered orally in one or more courses in doses of 100 to 125 mg. twice daily for 10 to 21 days, with a gradual reduction in dosage for five to seven days before the treatment was terminated. One patient received a total of 10.85 gm. of cortisone over a period of 77 days, as a form of long-term maintenance therapy (table 1), which was followed by 56 days of corticotropin therapy.

The characteristic euphoria and increase in appetite were noted in the successfully treated patients within the first week of therapy. These symptoms were associated with a prompt disappearance of the fever and a fall in the sedimentation rate and fecal lysozyme titer.

The initial response to hormone therapy was considered excellent in three patients, good in two, fair in two, and poor in one patient, who demonstrated no therapeutic effect.

The prompt effect of corticotropin therapy in inducing a symptomatic remission is demonstrated by patient B. B., a 41-year-old woman who had been semi-invalided for seven years with intermittent diarrhea, anemia, fever, and weight loss. Four months prior to admission, a large draining perianal fistula developed, associated with persistent diarrhea of 6 to 12 bloody mucoid evacuations daily, crampy abdominal pain, fever, chills, anorexia, and a weight loss of 16 lb. (7.3 kg.). Within one week

TABLE 1.—*Corticotropin and Cortisone Therapy in Ulcerative Colitis*

Patient	Courses of Treatment	Dosage, Mg./Day		Days of Treatment	Duration of Symptoms During Treatment		Interval from Initial Therapy to Proctoscopic Improvement (Days)	Results
		Corticotropin	Cortisone		Diarrhea (Days)	Gross Blood in Stools (Days)		
E. G.	1	80	...	18	6	6	22	Excellent
	2	..	200	14	21	21	None	Poor
		..	50	7	..	..	..	.....
		120	...	14	2	33	30	Fair
		40	...	19	..	(Trace)	..	.....
	3	..	250	21	..	..	..	.....
		..	150	7	7	40	..	.....
		..	100	7	..	(Occasional trace)	..	.....
		..	75	14	..	..	56	Good
		..	50	7	..	..	..	.....
		..	100	14	..	..	..	.....
		..	150	7	..	..	..	.....
		100	...	21	..	..	..	.....
		75	...	7	..	..	..	.....
		50	...	7	..	..	..	Excellent
		25	...	7	..	..	..	.....
		..	75	14	..	..	..	.....
O. D.	1	100	...	24	7-10	7-10	21	Excellent
		40	...	18	..	..	..	.....
B. F.	1	100	...	21	12-14	14	17	Excellent
	2	..	250	10	10	8-10	30	Good
	3	..	200	14	5	8	15	Good
A. M.	1	80	...	24	10-12	12-14	21	Fair
	2	100	...	16	7-10	7-10	25	Good
O. H.	1	80	...	11	11	11	..	Fair
		160	...	22	9	12	..	.....
		80	...	7	..	..	30	Good
		40	...	7	..	..	..	.....
L. B.	1	100	...	15	..	..	..	.....
		..	200	14	29	29	No change	Poor
H. I.	1	160	...	21	10	8	..	Good
	2	..	150	14	..	..	..	.....
H. E. N.	1	120	...	20	10	6	..	Good

RESULTS

Symptomatic Improvement.—A definite and occasionally dramatic remission was observed in five of the six patients with ulcerative colitis treated with corticotropin or cortisone during the acute phase of the disease. A similarly satisfactory remission occurred in the two patients with intractable diarrhea in the chronic phase. Unrelenting diarrhea, which had persisted for many months in spite of previous therapy, decreased significantly within the first two weeks of treatment and was usually brought under complete control within two to three weeks if the dosage of corticotropin or cortisone was adequate (table 1). There was an accompanying diminution or disappearance of blood in the stools, with marked relief of abdominal pain and tenesmus. One patient (L. B.) failed to respond to treatment.

of corticotropin therapy the diarrhea subsided, so that there were only two to four semiformed evacuations daily, and the patient experienced a sense of well-being and a remarkable increase in appetite. Two weeks after therapy was instituted, the nocturnal diarrhea and abdominal distress disappeared, and the stools became formed and were free of gross blood. The temperature, which had varied from 99 to 102 F daily, fell to normal within two days of treatment, and the sedimentation rate fell from 49 mm. per hour to 10 mm. within one week after the therapy was begun (fig. 1, table 1).

The perianal fistula decreased rapidly from 10 mm. in diameter to 6 mm. within three weeks of treatment. The drainage from one fistula diminished considerably, and the fistula regressed further to 2 mm. in diameter at the end of six weeks.

A similarly dramatic effect was observed in patient O. D., who complained of fecal incontinence for four months, with 10 to 18 blood-stained watery evacuations daily associated with marked tenesmus, a low-grade fever, and a 25 lb. (11 kg.) weight loss, in spite of prolonged hospitalization and intensive medical therapy, including the use of detergents and antibiotics and psychotherapy. Within one week of corticotropin therapy, the number of evacuations decreased to five and became semiformed. By the end of the second week the patient was passing one to three formed stools daily, which were free of occult blood. This was the first time in four months that the diarrhea had been controlled (table 1, figure 2). The tenesmus and abdominal pain diminished greatly within the first week and disappeared by the end of the second week of treatment. The characteristic euphoria and increased appetite were noted soon after therapy was instituted, and the patient gained 10 lb. (4.5 kg.) within one month.

Four additional patients with previously intractable diarrhea of four to six months' duration responded satisfactorily within 6 to 14 days of corticotropin administration (E. G., O. H., H. I., and H. E. N., table 1). A definite but less dramatic improvement was observed in patient A. M. (table 1), with disappearance in the nocturnal diarrhea within two weeks of treatment in spite of a rectal stricture, arthralgia of the knees and elbows, fever, and a 30 lb. (13.5 kg.) weight loss over a period of five months. No clinical response to corticotropin or cortisone therapy was observed in one patient during an acute severe exacerbation of chronic ulcerative colitis of 23 years' duration, extensive fibrosis and cicatrization of the colon, multiple strictures, and perianal and perineal fistulas (L. B., table 1).

In most patients the gross and occult blood in the stools diminished significantly within the first two weeks of treatment, during which time the diarrhea subsided (table 1). The stools became free of occult blood within 10 days of corticotropin therapy in two patients with ulcerative colitis in whom gross blood had been observed consistently for three to four months (O. D. and E. G., table 1). Occult blood in the stools persisted, however, for two to four months after treatment in several patients, (E. G., B. F., and O. H., table 1) and presented aserious problem in one patient (A. M.), in whom polyps in the transverse colon were demonstrable by x-ray. The bleeding appeared to be aggravated by hormone therapy during a severe relapse in one instance. This patient required multiple blood transfusions and responded satisfactorily to a subsequent prolonged course of corticotropin and cortisone therapy supplemented by antibiotics (E. G., table 1).

The profound and intractable anorexia and persistent weight loss that characterizes patients with severe ulcerative colitis presents a most difficult challenge in their management. Corticotropin or cortisone given in adequate dosage produced a consistent and impressive increase in the appetite and sense of well-being, which frequently heralded the remission in these malnourished, dehydrated patients. Although all the patients studied had lost weight consistently prior to treatment, a definite gain in weight could be demonstrated usually within the first three weeks of therapy. This weight gain continued for many weeks and months thereafter in all the patients who responded satisfactorily. Although some of the initial increase in weight was probably caused by retention of fluid, the long-term gain of weight, varying from 10 to 40 lb. (4.5 to 18.1 kg.), appeared to be initiated by the hormone treatment.

The increase in appetite was accompanied by disappearance of fever and a fall in the sedimentation rate usually within a few days of therapy. Increase in the hematocrit, plasma proteins, and body weight were observed later in the course of treatment.

Sigmoidoscopic Evidence of Healing.—Definite evidence of healing on sigmoidoscopic examination usually did not appear until after three weeks of hormone treatment. A consistent lag was observed between the clinical and sigmoidoscopic reflection of improvement in the disease.

Significant evidence of remission was observed on sigmoidoscopic examination in four patients. Pinpoint

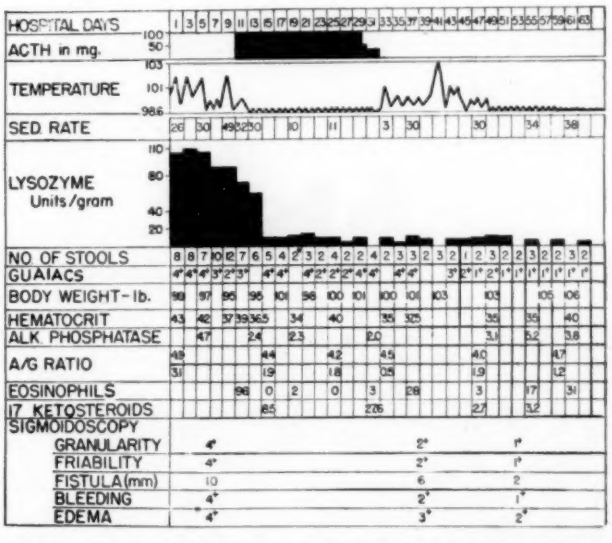

Fig. 1.—Effect of corticotropin on ulcerative colitis in patient B. F. (Asterisk signifies appearance of formed stools on day noted and thereafter.)

bleeding and diffuse ulceration were, in some instances, spectacularly decreased, and the mucosa appeared distinctly less friable, with markedly diminished granularity. In one patient (E. G.) the mucosa appeared essentially normal except for evidence of fine granularity after three weeks of treatment. This patient had a severe relapse, however, two months later. In no instance did the mucosa revert to normal within the first three to four weeks of treatment.

Patient O. D. demonstrated marked improvement and evidence of healing after three weeks of treatment, although minor residual granularity and bleeding were still present. A small single inflammatory pseudopolyp, seen on two occasions in the rectal mucosa, disappeared within three weeks. Six months later, the mucosa was indistinguishable from normal. This patient has remained in remission for 28 months (fig. 2, table 1).

There was no improvement in the appearance of the rectal mucous membrane of patient L. B., with multiple strictures, polyposis, and fistulas, in spite of treatment

with corticotropin and cortisone (table 1). A rectal stricture noted during the examination of another patient (A. M.) persisted after treatment, although it appeared less edematous. The amount of hormone necessary to induce evidence of healing observable on proctoscopic examination varies considerably. No evidence of healing was observed in patient E. G., during a severe relapse, while he had received 3,150 mg. of cortisone over a period of 21 days and 1,680 mg. of corticotropin during an additional 14-day period (table 1).

Roentgenologic Appearance.—An increase in the caliber and length of the colon, increase in haustral markings, and a more normal mucosal pattern were demonstrated in three patients (B. F., A. M., and O. D.) two months after treatment was instituted. There was no significant change in the roentgenographic appearance of the colon in the remaining patients with ulcerative colitis except for some diminution of spasm, motility and irritability. In no instance did the roentgenographic appearance return completely to normal.

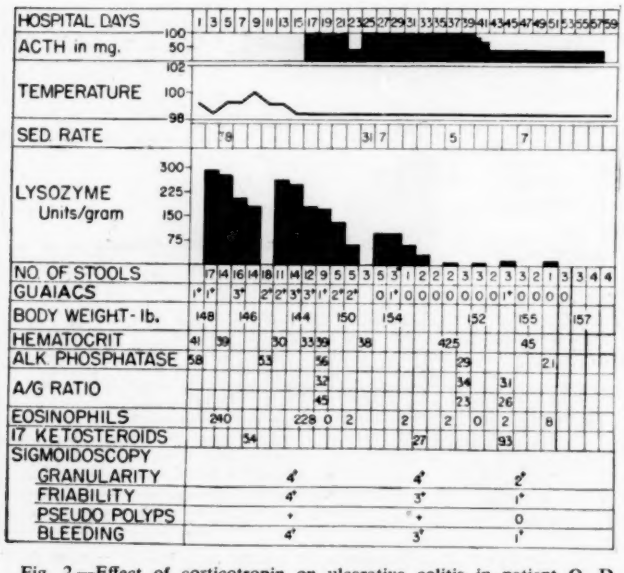

Fig. 2.—Effect of corticotropin on ulcerative colitis in patient O. D. (Asterisk signifies appearance of formed stools on day noted and thereafter.)

Decrease in Fecal Lysozyme.—Lysozyme is a mucolytic enzyme present in the colonic mucosa and other tissues in the body.[4] The fecal lysozyme titer is significantly elevated during the acute phase of ulcerative colitis and falls to low values approaching the normal range during the chronic inactive or remission phase. The mean lysozyme titer of 24 patients with active ulcerative colitis was 100 units per gram. In a series of 29 patients in the chronic inactive or remission phase, the mean lysozyme titer was 11 units per gram, compared with 5 units observed in 30 normal subjects (table 2). Studies in our laboratory indicated that the lysozyme titer paralleled the course of the disease and reflected its activity, decreasing with remissions and increasing with exacerbations.[5]

A marked fall in the fecal lysozyme titer occurred within 4 to 17 days of hormone treatment and coincided with the clinical improvement of the patient. This decrease in fecal lysozyme titer to the inactive remission

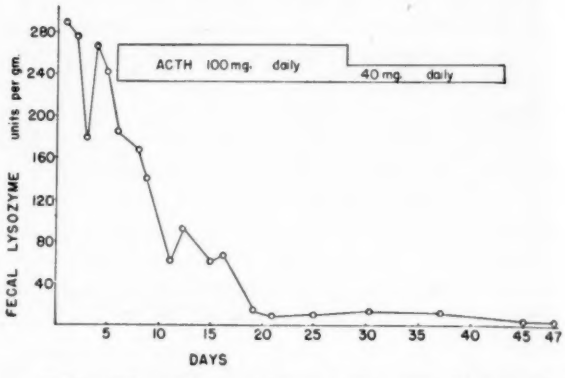

Fig. 3.—Effect of corticotropin on fecal lysozyme in patient O. D.

level following corticotropin therapy was observed uniformly in all patients responding satisfactorily to treatment. The mean lysozyme titer prior to hormone therapy was 133 units per gram, falling to 27 units per gram during the course of corticotropin administration, with subsequent levels of 16 units per gram at the end of treatment and during the consequent remission in the disease (table 2).

The decrease in fecal lysozyme titer paralleling the clinical course of the disease during corticotropin therapy is demonstrated in patient O. D. (fig. 2 and 3), in whom the titer fell from the pretreatment level of 291 units per gram to the chronic inactive level of 7 units on the 20th day of treatment, coincident with the remission. The lysozyme titer remained below 5 units for the subsequent 20 months.

The rapid clinical improvement in patient B. F. during corticotropin therapy was also reflected by a precipitous fall in the fecal lysozyme titer from a mean level of 97 units per gram before treatment to 9 units within four days of hormone therapy (fig. 1).

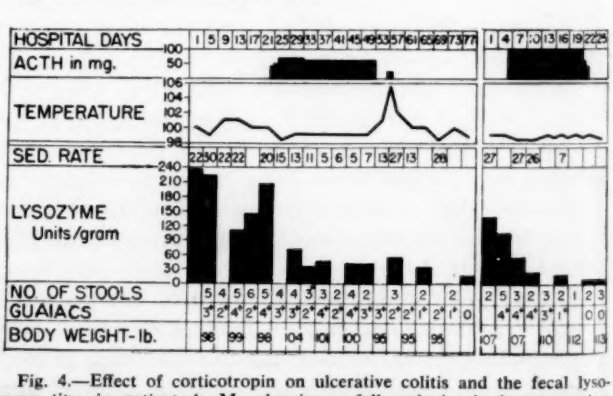

Fig. 4.—Effect of corticotropin on ulcerative colitis and the fecal lysozyme titer in patient A. M., showing a fall and rise in lysozyme titer paralleling the clinical remission and relapse of the disease. (An interval of 18 weeks elapsed between the hospital admissions. Asterisk denotes appearance of formed stools on day noted and thereafter.)

The relationship between the lysozyme titer and the activity of the disease was seen in patient A. M., who responded to corticotropin therapy but had a relapse 18

4. Meyer, K.; Gellhorn, A.; Prudden, J. F.; Lehman, W. L., and Steinberg, A.: Lysozyme Activity in Ulcerative Alimentary Disease: II. Lysozyme Activity in Chronic Ulcerative Colitis, Am. J. Med. **5**: 496, 1948.

5. Gray, Reifenstein, Connolly, Spiro, and Young.[1a] Gray, S. J.; Reifenstein, R. W.; Benson, J. A., Jr., and Young, J. C. G.: Treatment of Ulcerative Colitis and Regional Enteritis with ACTH: Significance of Fecal Lysozyme, A. M. A. Arch. Int. Med. **87**: 646 (May) 1951.

weeks later. The remission and subsequent relapse of the disease were paralleled by a fall and a secondary rise in the lysozyme titers. The fecal lysozyme fell from 220 units during the acute phase before treatment to 13 units during the remission. The lysozyme titer rose again to 110 units with the recrudescence of the disease and fell to 10 units after the second course of corticotropin and the resulting second remission, 14 days later (fig. 4).

With extensive cicatrization of the bowel, no therapeutic response may be anticipated. This was demonstrated in patient L. B., with extensive fibrosis of the colon, multiple rectal strictures, and perianal fistulas. This patient failed to demonstrate any significant effect of corticotropin or cortisone therapy on the fecal lysozyme titer or the clinical course of the disease.

LONG-TERM RESULTS

Relapses and Remissions.—Three patients have remained in good remission for 14 to 28 months following discontinuation of hormone therapy. A fourth patient, whose treatment was completed 10 months ago, is still in remission. Definite relapses occurred, however, two to nine months after treatment in the remaining three patients.

Patient O. D. had received an initial course of treatment consisting of 3,120 mg. of corticotropin over a period of 42 days (fig. 2, tables 1 and 3). He experienced an excellent clinical response and has remained in remission for 28 months without dietary restriction, works regularly, has one formed bowel movement daily, and has gained 45 lb. (20.4 kg.). Although x-ray studies reveal residual narrowing, shortening of the colon, and lack of haustration, the proctoscopic examination presents an essentially normal mucous membrane, with only mild residual granularity and thickening. This 46-year-old man had been completely incapacitated for seven months prior to treatment.

A 29-year-old lawyer, who was incapacitated for six months by bloody diarrhea (8 to 10 evacuations daily), which persisted in spite of adequate medical and psychiatric therapy, was treated with 5,240 mg. of corticotropin over a period of 47 days. He had a satisfactory remission, which has persisted for 14 months. He is able to work every day, has gained 25 lb. (11.3 kg.) in spite or two or three formed and semiformed small evacuations daily. Proctoscopically the mucous membrane presents the picture of healed ulcerative colitis. Insufficient time has elapsed to evaluate the permanency of this remission (tables 1 and 3).

A similarly satisfactory remission has been maintained by patient H. I. for 15 months after a 21-day course of corticotropin therapy (160 mg. daily) followed by 14 days of cortisone therapy (150 mg. daily). This 33-year-old man regularly works, has gained 30 lb. (13.6 kg.), and has two or three semiformed or formed evacuations daily. The mucosa appears healed on sigmoidoscopic examination. This patient had been unable to work for six months because of persistent diarrhea and weight loss (tables 1 and 3).

Ten months have elapsed since patient H. E. N. was treated (reported in detail under complications). There has been a 22 lb. (10 kg.) weight gain and the patient passes one or two formed stools daily.

Patient A. M., who had responded satisfactorily to three weeks of treatment with corticotropin (80 mg. daily), had a recurrence of diarrhea, with gross blood in the evacuation four months later. This 50-year-old woman had been bedridden for five months prior to hormone therapy because of uncontrollable diarrhea, tenesmus, 30 lb. (13.6 kg.) weight loss, severe anemia, and arthritis. The patient was given a second course of corticotropin therapy (100 mg. daily) for 16 days and responded again to treatment. This patient has remained in remission for 12 months since the last course of cortisone therapy without significant relapse and has gained 35 lb. (15.9 kg.). Occult blood in the stools and anemia have persisted, however, presumably because of polyps in the transverse colon demonstrated by x-ray. The patient has

TABLE 2.—*Fecal Lysozyme in Ulcerative Colitis Demonstrating the Effect of Corticotropin Therapy in Reducing the Lysozyme Titer to Inactive or Remission Levels*

	No. of Cases	Mean Lysozyme Titer (Units/Gm.)
Normal	30	5
Ulcerative colitis *		
Active	24	100
Inactive or healed	29	11
Ulcerative colitis †		
Before corticotropin therapy	7	133
After corticotropin therapy	7	16

* Previously reported; no hormone therapy was administered.[1]
† Present series of patients.

TABLE 3.—*Remissions and Relapses Following Hormone Therapy*

Patient	Courses of Treatment	Hormone	Days of Hormone Therapy	Duration of Remission After Therapy	Weight Gain (Lb.)	Relapse
E. G.	1	Corticotropin	18	2 mo.	10	Severe
	2	Cortisone	54	2 weeks	0	Severe
	3	Corticotropin Cortisone Corticotropin	133	3 mo.	20	None
O. D.	1	Corticotropin	42	28 mo.	45	None
B. F.	1	Corticotropin	21	9 mo.	30	Mild
	2	Cortisone	10	4 mo.	5	Mild
	3	Cortisone	14	8 mo.	..	.....
A. M.	1	Corticotropin	24	4 mo.	25	Moderate
	2	Corticotropin	16	12 mo.	10	.....
O. H.	1	Corticotropin	47	14 mo.	25	None
L. B.	1	Corticotropin	29	None	0	Ileostomy
H. I.	1	Corticotropin	21	15 mo.	30	None
	2	Cortisone	14	.....	..	.....
H. E. N.	1	Corticotropin	20	10 mo.	22	None

four or five formed or semiformed evacuations daily, and her weight gain has been maintained. She carries on her regular activities without significant limitation. Proctoscopic examination reveals a rectal stricture, with some thickening of the mucous membrane and fine granularity but no friability or gross bleeding. Appetite and sense of well-being remain excellent (tables 1 and 3).

A definite relapse occurred in patient (B. F.) nine months after corticotropin therapy. Although transient episodes of diarrhea followed dietary indiscretion during the remission, the patient had gained 30 lb. (13.6 kg.) and passed two formed stools daily without blood. Her appetite had remained excellent, and she was essentially asymptomatic and able to carry on her regular duties. Sigmoidoscopy revealed a thickened, healed, finely granular mucous membrane and a small persistent fistula. The relapse was characterized by severe bloody diarrhea

with urgency, temperature rises to 102 F, nausea and vomiting, and persistent anorexia. The patient was treated with 125 mg. of cortisone orally twice daily for 10 days and had a prompt remission within three days of cortisone administration, with a return of appetite and control of the diarrhea. Proctoscopic examination revealed healed ulcerative colitis in the remission phase.

A similar relapse associated with a 10 lb. (4.5 kg.) weight loss occurred four months later. A third course of cortisone, consisting of 100 mg. twice daily for 14 days, was administered. The diarrhea and fever subsided within five days, and the patient's appetite immediately improved. Since this last relapse the patient has been passing three formed stools daily and her appetite and sense of well-being continue to be excellent. Proctoscopic examination again revealed a healed inactive ulcerative colitis. The hematocrit is normal and the stools are free of occult blood (tables 1 and 3, fig. 1).

A very severe relapse characterized by diarrhea with massive hemorrhage, profound anorexia, and fever following prolonged physical exertion occurred two months after corticotropin treatment was discontinued in patient E. G., who had previously experienced an excellent and dramatic response to corticotropin therapy (tables 1 and 3). Treatment with cortisone, 200 mg. a day for 14 days, followed by 120 mg. of corticotropin daily for 14 days, resulted in some improvement. The patient was then maintained on 40 mg. of corticotropin daily for an additional period of 19 days. Two weeks after corticotropin therapy was discontinued, the patient experienced another severe relapse, which responded dramatically to cortisone therapy (125 mg. twice daily orally for three weeks, followed by smaller doses over a period of eight additional weeks).

LONG-TERM MAINTENANCE THERAPY

The rationale for long-term maintenance therapy and repeated courses of hormone treatment is demonstrated by the following case of fulminating ulcerative colitis, characterized by repeated episodes of massive hemorrhage, intractable diarrhea, profound anorexia, and weight loss with high temperature and leukocytosis, which was sustained in partial remission by three courses of corticotropin and cortisone therapy over a period of 11 months (tables 1 and 3). This desperately ill patient received a total of 11,900 mg. of cortisone and 3,150 mg. of corticotropin in 133 consecutive days, to prevent a relapse during the third course of treatment.

CASE 1.—E. G., a 17-year-old school boy, who was a long-distance runner, was admitted to the hospital on June 25, 1950, because of diarrhea, consisting of 10 to 12 watery, blood-tinged or grossly bloody stools per day of four months' duration. Diarrhea and blood loss were aggravated by strenuous exercise and stress associated with his racing activities and were accompanied with abdominal distress, tenesmus, and a 10 lb. (4.5 kg.) weight loss. Previous medical management did not appear to alter the severity of the diarrhea or the abdominal distress.

Physical examination disclosed no abnormalities except for evidence of weight loss and dehydration. The hematocrit was 43%, serum albumin 3.9 gm., and globulin 2.1 gm. per 100 cc., corrected sedimentation rate 21 mm. per hour, eosinophil 756 per cubic millimeter, and urinary 17-ketosteroid excretion 9.1 mg. per 24 hours. The stools contained gross blood and revealed no enteric pathogens on culture. The fecal lysozyme titer was 86 units per gram.

Proctoscopy showed a markedly friable, ulcerated, coarsely granular rectal mucosa, with pinpoint bleeding throughout. The patient was placed on a regular hospital diet for seven days, during which time the diarrhea and gross blood persisted.

Administration of corticotropin, 20 mg. every six hours, was begun on his seventh hospital day, and the patient was treated for 18 days, with a gradual diminution in the dose for the next three days. Within 24 hours his stool frequency diminished to two daily. Grossly visible blood disappeared on the sixth day of treatment, and the stools became formed for the first time in three months. On the 13th day of therapy his stools became guaiac negative. Corticotropin was the only medicament administered. It induced the usual eosinopenia (19 eosinophils per cubic millimeter) within three days and a urinary 17-ketosteroid increase to 20.9 mg. per 24 hours within seven days. The sedimentation rate fell to 12 mm. in one week, and the fecal lysozyme decreased to 4 units per gram within two days of corticotropin therapy.

The patient experienced pronounced euphoria and a ravenous appetite and gained 5 lb. (2.3 kg.) in two weeks. He was discharged on July 22 with one or two formed evacuations daily, free of occult blood. On the day of discharge the rectal and sigmoid mucosa was indistinguishable from normal.

After discharge, the patient did well except for occasional slight rectal bleeding after extensive exertion. His appetite remained good, and he continued to gain weight. In the middle of September, 1950, the patient began training again for long distance, cross country running. Three days later he noticed the onset of severe diarrhea and bleeding, with six or seven watery bowel movements daily, containing gross blood, and associated with severe anorexia, fatigue, and lower abdominal pain. On Oct. 3 he noticed an elevation in temperature to 102 F, and on Oct. 4 he was readmitted to the hospital.

On admission the patient weighed 94 lb. (42.6 kg.), appeared acutely ill, and had an elevation in temperature varying from 100 to 102 F. Physical examination revealed abdominal tenderness in both the right and the left lower abdominal quadrants. On proctoscopic examination, a diffusely granular, ulcerated, freely bleeding, very friable mucous membrane was observed. Free blood gushed from the mucosa and obscured the field at frequent intervals. Hematocrit was 34% and the sedimentation rate 33 mm. per hour. The white blood cell count was 18,600. The fecal lysozyme titer had risen to 88 units per gram.

Two hundred milligrams of cortisone was administered daily in divided doses for 14 days (Oct. 4 to 18), and then the dose was gradually tapered off to 25 mg. daily during the subsequent six days. During this period the patient continued to have a temperature elevation to 100 F daily, his anorexia and diarrhea persisted, and he continued to lose weight, so that on Oct. 17 his weight had decreased to 90 lb. (40.8 kg.), and the hematocrit continued to fall to 29% in spite of an adequate eosinophil response. Corticotropin therapy was begun on Oct. 18, the patient receiving 80 mg. daily in four divided doses for four days and 120 mg. a day for 10 days. Then the dose was tapered off to 40 mg. daily.

The characteristic sense of well-being, increased appetite, decrease in the number of stools, and prompt fall in temperature did not occur until the dose was increased to 120 mg. a day, after which a prompt remission occurred. After five days of the increased dose of corticotropin, the patient felt exceedingly well, remained afebrile, and had three formed and semiformed evacuations daily, all containing occult blood.

The patient continued to show improvement with corticotropin administration, regained the weight he had lost during the first part of his hospitalization, and was discharged on Nov. 5, weighing 95 lb. (43.1 kg.). The hematocrit on discharge was 34%, and the stool reactions were consistently positive for occult blood.

Proctoscopic examination on Nov. 6 revealed considerable improvement in the appearance of the mucosa. The lower 4 in. (10 cm.) of the rectal mucosa appeared almost normal. There was some fine granularity but no bleeding or friability. At the junction of the rectum and sigmoid, on the right lateral wall, the mucosa was hyperemic and very friable and bled profusely on trauma. This was localized to an area approximately 1 in. (2.5 cm.) in diameter. It was felt that the patient's improvement

in general, however, had been excellent, in view of the fulminating course of the disease.

The patient continued to improve while receiving 40 mg. of corticotropin daily in divided doses. He had three or four semiformed evacuations daily without gross blood, and his hematocrit rose to 38%.

Corticotropin treatment was stopped on Nov. 21. The patient continued to do well until Dec. 5, at which time he began to have severe diarrhea, five or six watery bowel movements a day with profuse gross blood. In spite of three transfusions and chloramphenicol (chloromycetin®) therapy, the course continued downhill, and the hematocrit on Dec. 19 was 29%. He had almost complete anorexia, and his weight on Dec. 26 had fallen to 85 lb. (38.6 kg.). The fecal lysozyme titer was 110 units per gram. X-rays revealed extensive serration, loss of haustration, and narrowing of the entire colon and rectum.

The patient refused hospitalization, although complete anorexia persisted. On Dec. 26 oral administration of cortisone, 125 mg. every 12 hours, was begun along with potassium chloride (0.9 gm. three times daily), and the patient was given another blood transfusion. By Jan. 2 (one week later) he noted a definite increase in appetite and a decrease in diarrhea and blood loss. He continued to improve, and by Jan. 16 he was passing two to three semiformed stools daily without gross blood. His appetite had improved tremendously, and he had gained 12 lb. (5.4 kg.) in three weeks. The dose of cortisone was decreased to 75 mg. twice daily on Jan. 16 and 50 mg. twice daily on Jan. 23.

The patient continued to improve and gain weight. The dose of cortisone was decreased further to 75 mg. daily, on Jan. 30. The dose was reduced to 50 mg. daily on Feb. 13. Within four days the diarrhea recurred and the patient noticed loss of appetite again. The hematocrit, however, was 38 on February 20, and there was no marked change on proctoscopic examination. The dose of cortisone was increased to 100 mg. daily, and there was an immediate return of appetite and diminution of diarrhea within a week. On March 6 cortisone was increased to 150 mg. daily, because the patient had failed to gain weight, although he was asymptomatic.

Beginning March 13, since cortisone was no longer available, the patient received decreasing doses of cortisone, 150 mg. for two days, then 100 mg., and finally 50 mg. Cortisone therapy was discontinued on March 20. Simultaneously with the decrease in cortisone dosage, on March 13, corticotropin therapy was begun, 100 mg. daily in divided doses. This was maintained for three weeks and then gradually decreased weekly to 75, 50, and finally 25 mg. daily. As the corticotropin dose was diminished the patient was given an oral antibiotic gantrisin® (3,4-dimethyl-5-sulfanilamido-isoxazole) 1.0 gm. four times daily.

The patient continued to improve and gain weight. On April 24 he weighed 113 lb. (51.3 kg.), representing a gain of 28 lb. (12.7 kg.) in four months. He was passing one to two formed stools daily without gross blood, and the hematocrit was 38. The proctoscopic examination revealed a finely granular mucous membrane, with no free bleeding or friability, indicating a healing process.

Comment.—Without hormone therapy, ileostomy would probably have been inevitable in this patient, in view of the massive bleeding and the profound weight loss and anorexia. The remission induced and sustained by corticotropin and cortisone therapy constituted excellent preparation of this patient for this procedure had it been necessary. The most marked beneficial clinical effect was on the patient's appetite and diarrhea. As soon as the dose of cortisone was reduced to less than 75 mg. daily, he noted an immediate decrease in appetite and increase in the number of evacuations.

The striking relationship of the fecal lysozyme titers to remissions and exacerbations of the disease was demonstrated by the decrease from pretreatment levels of 86 units to 5 units within five days of corticotropin therapy, coinciding with the clinical improvement. The lysozyme titer remained normal for two months during the remission period, only to increase to 78 units per gram with the recurrence of bleeding and diarrhea.

The effect of hormones on bacterial and inflammatory processes may be of considerable importance in patients with ulcerative colitis, who commonly have extensive secondary infection in the wall of the colon. It is advisable to administer antibiotics to these patients in order to decrease the bacterial flora of the intestine, particularly during the end of treatment. This may be important in the presence of bleeding. The use of antibiotics in conjunction with hormones appeared to decrease the amount of blood loss.

In long-term maintenance therapy with corticotropin or cortisone, the dose was reduced gradually over a period of one week before discontinuance of treatment in order to prevent adrenal suppression. This is particularly important with cortisone therapy. It may be advisable to alternate courses of corticotropin and cortisone therapy for the same reason as was done in patients E. G. and B. F. (table 1).

The occurrence of gastric hemorrhage and the development, reactivation, or perforation of peptic ulcers during long-term maintenance hormone therapy have been reported by a number of investigators.[6] Since these complications probably result from an increase in gastric acidity and pepsin,[7] the use of antacids may be indicated in these instances. Peptic ulcer contraindicates long-term hormonal maintenance therapy.

COMPLICATIONS

A temporary increase in the fasting blood sugar to 300 mg. per 100 cc. was observed in one patient (A. M.) within two weeks of corticotropin administration, with return to normal levels within 14 days of the discontinuation of the hormone therapy. No hyperglycemia was observed, moreover, during a subsequent course of corticotropin therapy, four months later. The effects of corticotropin and cortisone-like hormones on carbohydrate metabolism are usually temporary and do not constitute a danger except in patients with diabetes or diabetic tendency. The fasting blood sugar in this patient has remained normal for one year after treatment. This patient also had sterile subcutaneous abscesses and a virus pneumonia on discontinuation of corticotropin therapy. These complications responded satisfactorily to antibiotic and supportive therapy and did not appear to affect the colitis adversely.

Other complications were moderate hirsutism, acne, and pigmentation, which gradually disappeared after corticotropin treatment was terminated (B. F.).

Roundness of the face was observed in all patients during the second to third week of treatment. This varied in degree and diminished gradually after discontinuation of therapy.

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6. Habif, D. V.; Hare, C. C., and Glaser, G. H.: Perforated Duodenal Ulcer Associated with Pituitary Adrenocorticotropic Hormone, (ACTH) Therapy, J. A. M. A. **144**: 996 (Nov. 18) 1950. Kuzell, W. C., and Schaffarzick, R. W.: Cortisone Acetate in 32 Cases: Preliminary Clinical Observations, Stanford M. Bull. **8**: 125, 1950.

7. Gray, S. J.: Discussion on Treatment of Ulcerative Colitis, in Mote, J. R.: Proceedings of the Second Clinical ACTH Conference, Vol. II, Philadelphia, The Blakiston Company, 1951, p. 504. Gray, S. J.; Benson, J. A., Jr., and Reifenstein, R. W.: Chronic Stress and Peptic Ulcer: I. Effect of Corticotropin (ACTH) and Cortisone upon Gastric Secretion, J. A. M. A. **147**: 1529 (Dec. 15) 1951.

Fever immediately following the termination of corticotropin therapy was observed in B. F. and probably represented an exaggerated withdrawal effect. The eosinophil count increased, and the urinary 17-ketosteroid excretion fell from 27.6 to 2.7 mg. in 24 hours during the febrile period (fig. 1). No flare-up of the colitis resulted, however, and the temperature returned to normal without additional treatment within two weeks.

In the following patient (H. E. N.) a subphrenic abscess developed during corticotropin therapy, without any localizing physical findings on abdominal examination. This complication, however, did not appear to affect the remission in the disease process, which remained quiescent throughout this episode.

CASE 2.—H. E. N. (previously mentioned), a 50-year-old man, had had three attacks of ulcerative colitis over a period of 24 years. The last attack was in 1948, when the patient noted severe bloody diarrhea, consisting of 8 to 10 stools daily, tenesmus, meteorism, anorexia, and a 15 lb. (6.8 kg.) weight loss. He was treated with blood transfusions, bed rest, and antispasmodics, and the disease subsided gradually over a period of three months. The symptoms recurred 10 weeks prior to his present hospital admission, with the onset of explosive diarrhea (8 to 10 loose watery bowel movements daily), which did not respond to the usual medical management, including chloramphenicol therapy. He again complained of anorexia, nausea, cramping abdominal pain, tenesmus, and meteorism. Ileostomy was advised, in view of his intractable symptoms and chronic course.

On his admission to the hospital, the significant laboratory findings were a hematocrit of 34, white blood cell count of 9,300, and a sedimentation rate of 36. The blood chemistry findings were all normal. The stool guaiac was 4+ for blood, urinary 17-ketosteroids were 3.3 mg. in 24 hours, and the eosinophil count was 603 per cubic millimeter. The fecal lysozyme titer before hormone therapy was 104 units per gram. X-rays of the colon revealed pipe-like narrowing, with a fine ragged irregularity in outline of the entire colon and rectum. No normal haustrations could be seen.

The patient was observed for one week before corticotropin therapy was begun. On dietary management, sedation, and treatment with antispasmodics, he passed 9 to 10 watery, blood-stained stools daily. On Feb. 19, 1951, corticotropin therapy was begun, with 120 mg. daily in four divided doses, and 2.7 gm. of potassium chloride daily. All other medication was discontinued. The patient showed a good hormone response, with a fall in the eosinophils to 21 per cubic millimeter and an increase in 17-ketosteroids to 9.3 mg. in 24 hours. Within one week of hormone therapy, the patient noted a marked improvement in the diarrhea, so that by Feb. 25 he was passing one or two formed or semiformed stools daily. Within 10 days of treatment the abdominal distress completely disappeared, although occult blood in the stools still persisted.

On Feb. 28, after 10 days of corticotropin therapy (120 mg. daily), the patient began to complain of left costovertebral pain. Examination of the abdomen at this time revealed no evidence of spasm or tenderness. The white blood cell count, however, rose to 14,000, although there was no change in the sedimentation rate. The dose of corticotropin was decreased to 80 mg. daily on March 3 and discontinued, after a tapering-off process, on March 14. The patient received a total dose of 2.49 gm. over a period of 24 days.

An elevation of temperature to 100 F was observed for the first time on Feb. 3. The temperature returned to normal in three days. On March 14, the last day of corticotropin therapy, remittent fever to 102 F daily was observed and the patient continued to complain of left back pain. No effect was noted, however, on the colitis. The patient continued to pass two to three formed or semiformed stools daily, and the abdomen remained soft, without any evidence of localized spasm or tenderness. On March 17 the white cell count rose to 22,800. X-ray of the chest and abdomen revealed a large gas bubble and fluid level just below the left part of the diaphragm, presumably due to a large subphrenic abscess. Antibiotic therapy was instituted on March 14, and the abscess was drained surgically on March 30. The patient was discharged one week later, with an uneventful convalescence.

During this entire period the ulcerative colitis process appeared to remain in remission. Two weeks after surgery the patient was passing one or two formed stools daily, and in the subsequent two months he gained 22 lb. (10 kg.). There has been no evidence of a relapse since the institution of corticotropin therapy, in spite of this complication. The lysozyme content of the stools at the end of corticotropin therapy was 12 units per gram, which is characteristic of the remission phase of the disease.

Comment.—Since the tissue reaction to infection and inflammation is markedly altered by hormones, the possibility of infection as a complication in the management of ulcerative colitis with corticotropin or cortisone must be considered. Such complications were observed in A. M., in whom virus pneumonia and sterile subcutaneous abscesses developed at the end of her course of corticotropin therapy. The apparent perforation of a small ulcer in the colon with a resulting subphrenic abscess (H. E. N.) may also have resulted from decreased tissue resistance to infection and diminished localization of foci of infection by fibroblasts. There is a reasonable possibility that the increase in bleeding occasionally seen in patients with ulcerative colitis receiving corticotropin or cortisone may be also caused by a decrease in the inflammatory reaction on the part of the tissues to bacteria and bacterial toxins, with a subsequent increase in bleeding on an inflammatory basis (E. G.). The use of antibiotics in conjunction with hormone therapy in patients with ulcerative colitis is therefore indicated.

The absence of fever or abdominal rigidity in two cases in which acute peritonitis developed during treatment with corticotropin has been reported by Beck,[8] who emphasized the fact that acute perforation of an abdominal viscus with development of peritonitis may be obscured by treatment with corticotropin. Fever and leukocytosis developed in H. E. N., but there were no localizing signs whatever on abdominal examination, presumably because of hormonal inhibition of the reactivity of the tissue to inflammation. It is remarkable that the ulcerative colitis remained quiescent in spite of the perforation, development of abscess, and subsequent surgery.

COMMENT

Hormone therapy appeared to induce a significant symptomatic remission in seven of eight patients with ulcerative colitis who were completely incapacitated by their disease and refractory to other forms of medical management. The remission in no sense constitutes a cure, since sigmoidoscopic examination indicated incomplete healing in some instances and relapses occurred in three patients two to nine months after treatment. Nevertheless, the control of diarrhea, decrease in fecal blood loss, and marked increase in appetite and sense of well-being, which are attendant on adequate hormone therapy, make it an exceedingly valuable adjunct in the treatment of ulcerative colitis.

Further evidence that hormone therapy induces a remission in the disease is the significant fall in fecal lyso-

8. Beck, J. C.; Browne, J. S. L.; Johnson, L. G.; Kennedy, B. J., and MacKenzie, D. W.: Occurrence of Peritonitis During ACTH Administration, Canad. M. A. J. **62**: 423, 1950.

zyme titer within 4 to 17 days of corticotropin therapy to levels observed uniformly in patients in the chronic inactive or remission phase of the disease. Since the lysozyme titer is a measure of the activity of the disease process and parallels its clinical course, decreasing with remissions and increasing with exacerbations, the low levels observed after corticotropin therapy are significant. The fecal lysozyme titer, moreover, reflects the tissue reaction to injury or inflammation and is present in increased amounts in granulation tissue, pus,[9] and granulocytes.[10] The fall in fecal lysozyme during corticotropin therapy may reflect the inhibitory effect of corticotropin on the tissue's reaction to injury in which granulation tissue exudates and granulocytes play a part. It follows a similar pattern to the inhibition of other tissue reactions to injury, such as fibroblastic proliferation and production of tissue lymphocytes, gamma globulin, complement, and hyaluronidase.

A reduction in the urinary 17-ketosteroid levels prior to corticotropin therapy was observed in six of the eight patients studied. A normal rise in the urinary 17-ketosteroid levels, however, occurred with corticotropin administration, indicating a reduced activity but a normally responsive gland. This depletion in adrenal activity probably reflects prolonged inanition, malnutrition, and chronic stress associated with extensive disease (table 4).

Patients with marked adrenal depletion and very low urinary 17-ketosteroid excretion may not respond to treatment with the usual dose of corticotropin or cortisone. Patient L. B., with extensive cicatrization of the colon, multiple rectal strictures, and perianal and perineal fistulas, had the lowest urinary 17-ketosteroid excretion of all the patients treated and exhibited no clinical response or decrease in fecal lysozyme titer in spite of a 15-day course of corticotropin therapy (100 mg. daily) and 14 days of cortisone therapy (150 mg. daily).

The clinical response to hormone therapy appears to depend on adequate dosage, which varies considerably in different patients depending on the activity and duration of the disease, the ease with which the adrenal can be stimulated, and the state of depletion of the adrenal gland with consequent decrease in endogenous output of adrenal hormones. Spontaneous remissions in the disease may depend in part on the release of endogenous hormones. During the past year the intravenous administration of 20 mg. of corticotropin daily over an 8-hour period in 500 cc. of dextrose in water has proved very satisfactory.

Patient O. H. showed no clinical effect whatever to 80 mg. of corticotropin daily, in spite of a good blood eosinophil and urinary 17-ketosteroid response. When the dose of corticotropin was increased to 160 mg. daily for 22 days, he experienced an excellent remission, which has persisted for six months. Patient E. G. exhibited no clinical response to treatment with 200 mg. of cortisone daily for 14 days but reacted favorably to further treatment with 120 mg. of corticotropin daily for 14 days, followed by 40 mg. daily for 19 additional days. In general, the patients who received the largest doses of hormone had the longest remissions. Patient O. D., for example, who received 3,120 mg. of corticotropin over a period of 42 days, has been in excellent remission for 28 months.

SUMMARY AND CONCLUSIONS

1. The administration of corticotropin (ACTH) or cortisone to patients with extensive and intractable ulcerative colitis was accompanied by a significant and sometimes dramatic remission in seven of eight patients who were completely incapacitated by the disease and refractory to other forms of medical management.

2. A marked fall in the fecal lysozyme titer to levels observed in the inactive or remission phase of the disease accompanied the clinical remission and occurred within 4 to 17 days of corticotropin therapy in all patients responding to treatment.

3. Three patients have remained in remission for 14 to 28 months and have been restored to full activity.

4. Definite relapses occurred in three patients within two to nine months after hormone therapy. Repeated courses of corticotropin or cortisone induced satisfactory remissions in these patients.

5. No clinical response was observed in one patient with extensive cicatrization of the colon, multiple rectal strictures, and perineal and perianal fistulas.

TABLE 4.—*Urinary 17-Ketosteroid Excretion in Ulcerative Colitis*

Patient	Sex	Control Period Mg./ 24 Hr.	Corticotropin Therapy Mg./ 24 Hr.	Patient	Sex	Control Period Mg./ 24 Hr.	Corticotropin Therapy Mg./ 24 Hr.
B. F.	F	8.5	27.6	E. G.	M	9.1	20.9
L. B.	F	1.4	6.0	H. I.	M	3.3	....
A. M.	F	4.4	15.0	H. E.	M	8.6	30.0
		2.0	21.0	O. H.	M	6.0	19.7
				O. D.	M	5.4	27.0
	Normal	10.0	15-25		Normal	15.0	20-30

6. In one patient a perforation and subphrenic abscess developed during corticotropin therapy, without localizing spasm, rigidity, or tenderness on abdominal examination. The ulcerative colitis remained quiescent and in remission, however.

7. The efficacy of long-term maintenance therapy and repeated courses of treatment is discussed. One patient was sustained in remission with 11,900 mg. of cortisone and 3,150 mg. of corticotropin given over a period of 133 days.

8. Remissions induced by hormone therapy may prove of value in preparation of patients for surgery. The indications for use of antibiotics in conjunction with hormone therapy are discussed.

9. The dose requirement and duration of treatment must be individualized for each patient, depending on the clinical response, severity of the disease, and degree of adrenal depletion. The best long-term results were obtained in patients receiving a prolonged course of treatment.

10. Hormone therapy does not constitute a cure for ulcerative colitis but is a valuable adjunct in the treatment of this disease.

721 Huntington Avenue.

9. Prudden, J. F.; Lane, N., and Meyer, K.: Lysozyme Content of Granulation Tissue, Proc. Soc. Exper. Biol. & Med. **72**: 38, 1949.

10. Gottschall, G.: Personal communication to the author.

CLINICAL NOTES

CAUSES OF FAILURE IN TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS

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Richard Bader, M.D.
and
Charles K. Friedberg, M.D., New York

The recovery rate of patients with subacute bacterial endocarditis has increased progressively, but death from incomplete eradication of the infection or from complications of the disease still occurs in 20% to 30% of the patients.[1] It seems appropriate, therefore, that in every fatal case a careful scrutiny be made into the possible causes of failure, in the hope that the knowledge thus obtained may further improve the effectiveness of treatment.

The accompanying report deals with a patient who was admitted four times to the hospital for the treatment of the original episode of subacute bacterial endocarditis and, subsequently, for relapses following apparently adequate courses of treatment. An analysis was made to determine why this patient died despite the use of various antibiotics, singly and in combination, and despite large doses of those antibiotics, apparently adequate according to careful bacteriologic and sensitivity studies.

REPORT OF A CASE

A 56-year-old man was admitted to the Mount Sinai Hospital in September, 1949, with complaints of weakness, fatigue, and exertional dyspnea for three months. Four weeks earlier the patient was digitalized because of dyspnea on exertion and swelling of the legs and feet. One week before hospitalization he suddenly experienced bilateral lumbar pain, with radiation to the left groin, followed by a rise in temperature to 102 F. Physical examination revealed a pale, thin man with moderate orthopnea. The temperature was 100.4 F, pulse rate 92 per minute, and respirations 28 per minute. The blood pressure was 134/72. There were two small petechiae in the conjunctiva of the left lower lid. Rales were audible at the bases of the lungs posteriorly. There was a harsh systolic murmur at the cardiac apex, transmitted to the axilla, and also a short harsh systolic murmur over the aortic area. The liver was enlarged to a level 5 cm. below the right costal margin and was slightly tender. The spleen was palpable 1 cm. below the left costal margin. There was tenderness over the costovertebral angles.

Laboratory Examinations.—The blood cell count showed 8.7 gm. hemoglobin per 100 cc., 3,800,000 erythrocytes, and 7,600 leukocytes per cubic millimeter, with a normal differential count. The erythrocyte sedimentation rate was 49 mm. per hour (Westergren). The urine was acid with a specific gravity between 1.006 and 1.019 (average, 1.014). On microscopic examination there were 5 to 10 erythrocytes, 2 to 3 leukocytes, and occasional hyaline and granular casts per high power field. X-ray examination of the chest revealed considerable enlargement of the heart to the left. The electrocardiogram showed only RS-T and T wave changes consistent with digitalis effects. An intravenous pyelogram showed the kidneys to be of normal size, the urinary tracts to be poorly visualized, and the spleen slightly enlarged. The blood urea nitrogen was 44 mg. per 100 cc. and the urea clearance 17.8 and 21.7 cc. per minute. The thymol turbidity and cephalin flocculation tests both gave a 3+ reaction.

From the First Medical Service of The Mount Sinai Hospital.

1. Friedberg, C. K.: Subacute Bacterial Endocarditis: Revision of Diagnostic Criteria and Therapy, J. A. M. A. **144**: 527 (Oct. 14) 1950.

Three successive cultures of the blood revealed the presence of Streptococcus viridans, which was moderately sensitive to penicillin and more so to aureomycin and streptomycin according to in vitro studies (table 1).

Diagnosis.—The patient apparently had a rheumatic mitral and possibly aortic valvular lesion complicated by subacute bacterial endocarditis, as indicated by the association of fever, white-centered petechiae, splenomegaly, anemia, and renal embolization, and as confirmed by the culture of Str. viridans from the blood stream. In addition, there was congestive heart failure and renal insufficiency, the latter denoted by the poor concentration of the urine, the low urea clearance, and the azotemia.

Treatment.—Treatment was begun with procaine penicillin in aluminum monostearate. The patient received 1,200,000 units of procaine penicillin per day for nine days, after which the dosage was increased to 1,800,000 units per day because of the persistence of low grade fever, even though cultures of the blood were negative. After 19 days of this higher dosage, the dose was again increased to 2,400,000 units a day because of periodic low grade fever, and this dosage was continued for an additional 21 days. Thus the patient received a total of seven weeks of therapy, during which cultures of the blood were continuously negative. In addition, he was treated for congestive heart failure, with a satisfactory clinical response.

Second Admission.—Two months after leaving the hospital, the patient was readmitted because of a history of low grade fever and swelling of the ankles for two weeks, and the growth of Str. viridans in blood cultures made in a routine follow-up examination.

Examination again revealed fever, a cardiac murmur, anemia, microscopic hematuria, elevated erythrocyte sedimentation rate, three positive blood cultures for Str. viridans, and evidence of congestive heart failure and renal insufficiency.

In view of the relapse following penicillin therapy and the in vitro sensitivity to aureomycin, the patient was treated with aureomycin in doses varying between 4 and 2 gm. daily for a total of 56 days (table 2). During this period his blood cultures became negative, the temperature returned to normal levels in four days, and he felt subjectively improved. He experienced transient episodes of auricular fibrillation with continuous manifestations of mild congestive heart failure, which was treated with rest, low sodium diet, digoxin, and mercurial diuretics.

Third Admission.—Two weeks after his discharge from the hospital, the patient had a recurrence of pain in his left flank, associated with the passage of reddish brown urine. One week later a culture of his blood was positive for Str. viridans, and he was readmitted to the hospital in May, 1950.

Once again the patient presented the same clinical picture of fever, anemia, splenomegaly, cardiac murmur, cardiac enlargement, and signs of congestive heart failure. Further cultures of the blood grew the Str. viridans, which was sensitive to penicillin as well as to aureomycin, streptomycin, and chloramphenicol. In view of the previous failure with 2,400,000 units of penicillin daily, and in view of the possibility that the combination of penicillin and aureomycin might possess more effective bactericidal action than penicillin alone, the patient was given 4,800,000 units of penicillin intramuscularly and 4.0 gm. of aureomycin orally each day for a period of 14 days. Thereafter, because of intolerance to aureomycin, and because sensitivity studies failed to disclose any significant synergism of aureomycin and penicillin, the aureomycin therapy was discontinued and procaine penicillin therapy was continued intramuscularly for an additional 28 days with a daily dosage of 9,600,000 units. The penicillin blood level with this dose ranged up to 30 units per cubic centimeter of blood. Cultures of the blood were all negative; the patient again became afebrile, and his well-being increased. However, evidence of congestive heart failure persisted, with the development of chronic auricular fibrillation.

Fourth Admission.—The patient was readmitted two months later, in September, 1950, with the complaints of increasing dyspnea, swelling of the ankles, and insomnia, despite intensive treatment of his heart failure. Examination disclosed signs of advanced congestive heart failure. Fever was absent on this admission, and there were no petechiae or emboli. The hemoglobin

was 14.5 gm. per 100 cc. He was treated with oxygen, digoxin, and diuretics without avail. Cheyne-Stokes respiration appeared, and the patient died on the third day of hospitalization, approximately one year after his first admission.

Postmortem Findings.—Findings at autopsy were as follows: rheumatic heart disease, inactive with mitral valvulitis, and endocarditis of the left atrium; subacute bacterial endocarditis, healed and active, involving the mitral valve and wall of the left atrium; cardiac hypertrophy and dilatation (heart weight, 500 gm.) and myocardial fibrosis; mural thrombus of the right auricular appendage and embolism to a branch of the pulmonary artery supplying the upper lobe of the left lung; chronic passive congestion of the viscera, including the liver, spleen, kidney, gastrointestinal tract, and lungs, with moderate bilateral hydrothorax; congestive splenomegaly (spleen weight 400 gm.); healed Loehlein-Baehr lesions and mild arteriosclerosis of the kidneys. Microscopic examination showed bacteria in the valves.

COMMENT

In an analysis of previous fatal cases, errors in diagnosis, persistently negative cultures of the blood, which delayed diagnosis or hampered the choice of the appropriate antibiotic and adequate dosage, or isolation of a highly resistant organism seemed to account for many of the fatalities.[1] None of these factors appeared to apply in this case. Recent studies have indicated that the host

TABLE 1.—*Sensitivity of Streptococcus Viridans in Vitro**

Admission	Agent to Which Str. Viridans Proved Sensitive, Amount	Times as Resistant as Standard
1st	Penicillin, 0.3 unit/cc.	15
	Aureomycin, 0.2 μg/cc.	1
	Streptomycin, 0.6 μg/cc.	3
2nd	Penicillin, 0.5 unit/cc.	2½
	Aureomycin, 0.4 μg	2
	Streptomycin, 0.4 μg	2
3rd	Penicillin, 0.02 unit/cc.	1
	Aureomycin, 0.4 μg/cc.	2
	Streptomycin, 0.1 μg/cc.	½
	Chloramphenicol, 0.8 μg/cc.	1.6
	Completely inhibited by sulfadiazine, 1 mg./100 cc.	..

* There was no growth in the culture made on the patient's fourth admission.

factor of defense against the causative micro-organism and healing is rarely an effective mechanism in subacute bacterial endocarditis.[2] This is supported by the rarity of spontaneous cure of this disease prior to effective antibiotic therapy.[3] It has been suggested that with many diseases, such as lobar pneumonia, brief inhibition of growth of the pneumococci permits cellular and humoral host defenses to cure the disease. On the other hand, in subacute bacterial endocarditis, it appears necessary to kill virtually all the causative organisms to effect a cure, because the host defense is of minimal assistance.[2]

In view of these considerations, was adequate dosage of the appropriate antibiotic given? We must be guided by sensitivity studies in vitro, concentrations of the antibiotic in the blood, and the clinical response of the patient. The antibiotic therapy appeared clinically adequate in the second and third admission, when the temperature course was restored to normal and cultures of the blood were persistently negative. During the first admission, cultures of the blood were also negative after treatment was begun, but the temperature, although considerably reduced, occasionally ranged above normal. However, it is not uncommon to observe low grade fever during the period of penicillin administration in successfully treated patients.

With respect to sensitivity studies, a distinction should be made between bacteriostatic and bactericidal action. When the sensitivity of a micro-organism to a given antibiotic is ordinarily reported by the laboratory, it denotes

TABLE 2.—*Treatment in the Case Reported**

Admission	Drug	Daily Dose	Duration, Days	Antibiotic Level
1st	Penicillin with aluminum monostearate	1,200,000 units	4	2 units/cc.
	Penicillin with aluminum monostearate	1,800,000 units	19	5 units/cc.
	Procaine penicillin	2,400,000 units	27	5 units/cc.
	Total.....	103,800,000 units		
2nd	Aureomycin	4.0 gm.	13	4 μg/cc.
	Aureomycin	2.0 gm.	9	2 μg/cc.
	Aureomycin	3.0 gm.	34	5 μg/cc.
	Total.....	172.0 gm.		
3rd	Procaine penicillin	2,400,000 units	3	.....
	Procaine penicillin / Aureomycin	4,800,000 units / 4.0 gm.	14	.....
	Procaine penicillin	9,600,000 units	28	30 units/cc. (penicillin)
	Total.....	343,000,000 units of penicillin 56.0 gm. of aureomycin		

* No antibiotic therapy during the patient's fourth admission.

a bacteriostatic effect. Thus a sensitivity of 0.3 indicates inhibition of multiplication by 0.3 unit of penicillin per cubic centimeter. However, many organisms remain viable with this concentration of antibiotic and will continue to multiply if transplanted to fresh culture mediums or if penicillinase is added. It has been general practice in the treatment of subacute bacterial endocarditis to try to attain a bactericidal antibiotic concentration that is 5 to 10 times as great as that indicated by in vitro (bacteriostatic) sensitivity studies (table 3). The patient in this case suffered a relapse after his first period of treatment, although blood levels of penicillin were more than 5 and often more than 10 times the reported sensitivity of the causative Str. viridans (tables 1 and 2). Perhaps in this instance the bactericidal concentration, which was

TABLE 3.—*Results of Special Studies on Sensitivity and Synergism*

Antibiotic	Inhibition (Bacteriostatic)	Completely Killed (Bactericidal)
Penicillin	0.02 unit/cc.	0.8 unit/cc.
Chloramphenicol	0.8 μg/cc.	8.0 μg/cc.
Aureomycin	0.4 μg/cc.	4.0 μg/cc.
Streptomycin	0.1 μg/cc.	4.0 μg/cc.
Sulfadiazine	1 mg./100 cc.	Growth still present at 100 mg./100 cc.
Penicillin / Streptomycin	0.4 unit / 2.0 μg	0.72 unit / 3.6 unit
Penicillin / Aureomycin	0.32 unit / 1.6 μg	0.4 unit / 2.0 μg

not determined, was substantially more than 10 times the bacteriostatic level. Actually, on the third admission it was found that the bactericidal level was 40 times the bacteriostatic; that is, 0.8 unit of penicillin per cubic centimeter was needed to completely kill the organism while only 0.02 unit sufficed to inhibit growth.

2. Hunter, T. H.: Speculations on the Mechanism of Cure of Bacterial Endocarditis, J. A. M. A. **144**: 524 (Oct. 14) 1950.

3. Libman, E., and Friedberg, C. K.: Subacute Bacterial Endocarditis, ed. 2, New York, Oxford University Press, 1948.

The essentially bacteriostatic but not bactericidal action of the sulfonamides (table 3) accounts for the frequent temporary clinical remissions but only occasional cures, despite high dosage and prolonged administration that followed their use in the era before penicillin.[4] Aureomycin, also, is usually only bacteriostatic against the nonhemolytic streptococci, causing subacute bacterial endocarditis.[5] Although the patient received 172 gm. of aureomycin over a period of eight weeks, during which cultures of the blood were negative, and he appeared clinically asymptomatic, there was a prompt relapse after the antibiotic therapy was discontinued. In this hospital similar experience was encountered in 5 of 10 other patients treated with aureomycin.[5]

Careful studies were made on the third admission, both to determine the dosage of penicillin that would be expected to have a bactericidal action on the causative Str. viridans and to determine whether treatment with a combination of penicillin with some other antibiotic would be more effective than with either alone. A review of table 2 and table 3 will disclose that the blood concentrations of penicillin far exceeded the bactericidal level and should have sufficed to eradicate the infection. Furthermore, during two weeks of the total of more than six weeks, aureomycin was combined with penicillin. Notable synergistic effects had previously been reported with penicillin and streptomycin in the treatment of subacute bacterial endocarditis due to the highly resistant Enterococcus or Streptococcus fecalis [2] and more recently with aureomycin and streptomycin in the treatment of brucellosis.[6] However, combinations of antibiotics are not always more effective than the individual ones and may be less effective. Thus Jawetz and his associates [7] found that the use of chloramphenicol in combination with penicillin actually curtailed the bactericidal effect of penicillin alone on enterococci, and similar observations were made recently by Spicer.[8] The use of combinations of antibiotics is inadvisable except after careful preliminary bacteriologic study. In the case presented here such studies revealed that aureomycin did not increase the bactericidal effect and actually reduced the bacteriostatic effect of penicillin.

When death occurs from congestive heart failure, the bacterial infection of the heart valves may or may not be cured. If there is no evidence of active bacterial infection, the cardiac failure may be attributed to the nonspecific toxic effect on a rheumatic heart with low cardiac reserve, to activation of rheumatic inflammation, or to the direct valvular destruction and myocardial damage caused by the bacterial infection prior to cure. In this case there was no evidence of activation of rheumatic inflammation. On the other hand, as is often found in patients with subacute bacterial endocarditis dying of heart failure after the infection appears eliminated, postmortem examination disclosed that active bacterial infection was still present. This indicates that valvular and myocardial damage due to bacterial endocarditis had occurred not only prior to the first hospital admission, and in the brief periods between treatment when positive blood cultures were obtained, but continuously from the onset of the disease and throughout almost a year of repeated hospitalizations.

There is uncertainty as to the cause of the persistent bacterial infection in view of the relative sensitivity of the causative micro-organism and the seeming adequacy of appropriate antibiotic therapy. Perhaps the dosage of penicillin during the first period of treatment might now be regarded as not sufficiently generous, even though the blood cultures became negative and antibiotic levels of the blood appeared adequate. On the other hand, since the sensitivity of the organism to penicillin did not diminish, it might have been anticipated on the basis of numerous experiences in other cases that retreatment with the much larger doses that were subsequently given would have effected a cure.

It appears probable that the therapeutic failure in this case was not dependent on the character of the treatment or the promptness with which it was initiated in the hospital, but that it was predetermined by events prior to hospitalization. The onset of the patient's illness appeared to have occurred at least three months prior to his admission. The diagnosis of subacute bacterial endocarditis had not been entertained prior to hospitalization. The development of congestive heart failure one month prior to admission was probably the result of the valvular and myocardial lesions of bacterial endocarditis and denotes that the disease was already advanced at that time. Similarly, the presence of renal insufficiency at the time of the patient's first hospitalization also suggests the presence of advanced bacterial endocarditis. Previous studies have indicated that the mortality rate from subacute bacterial endocarditis increases substantially when the duration of the illness exceeds two months and that the presence of cardiac failure or renal insufficiency usually indicates late manifestations of the disease.

Our discussion thus far has been concerned with the adequacy of penicillin therapy in this case, and our conclusion was that treatment was probably adequate. This discussion presupposed that the antibiotics administered actually reached all the micro-organisms in the valves and other bacterial foci. However, pathological studies disclose that the bacteria are often deep seated in avascular valve tissue and that they may be protected from the action of blood and its contained antibiotic by substantial quantities of fibrin and degenerative necrotic tissue. The probability of such deep-seated bacterial lesions increases with the duration of the disease prior to the commencement of adequate treatment. In this as in other fatal cases of long duration prior to treatment, it seems probable that failure to eradicate the infection denotes failure of the antibiotic to reach such deep-seated bacterial foci even when the concentration of the antibiotic in the blood stream far exceeds the necessary bactericidal level. These considerations reemphasize the importance of

4. Lichtman, S. S.: Treatment of Subacute Bacterial Endocarditis: Current Results, Ann. Int. Med. **19**: 787, 1943.

5. Friedberg, C. K.: The Treatment of Subacute Bacterial Endocarditis with Aureomycin, J. A. M. A. **148**: 98 (Jan. 12) 1952.

6. Herrell, W. E., and Barber, T. E.: A New Method for Treatment of Brucellosis, J.A.M.A. **144**: 519 (Oct. 14) 1950.

7. Jawetz, E.; Gunnison, J. B., and Coleman, V. R.: The Combined Action of Penicillin with Streptomycin or Chloromycetin on Enterococci in Vitro, Science **111**: 254, 1950.

8. Spicer, S.: Bacteriologic Studies of the Newer Antibiotics: Effect of Combined Drugs on Microorganisms, J. Lab. & Clin. Med. **36**: 183, 1950.

early diagnosis and early treatment before deep, inaccessible bacterial lesions are formed and before extensive myocardial and valvular damage occurs. The fact that patients are rarely hospitalized before they have been ill for six weeks indicates that the problem primarily concerns the general physician practicing outside the hospital.

SUMMARY

This is a report of a case of subacute bacterial endocarditis in which death occurred from congestive heart failure after three courses of therapy that seemed effective during each period of observation. Despite the use of penicillin and aureomycin, singly and in combination in apparently adequate dosage, and despite an apparent bacteriologic cure during life, postmortem examination disclosed active bacterial lesions in the valvular and mural endocardium.

An analysis was made to determine the possible factors responsible for this therapeutic failure. It was concluded that the prolonged duration of the undiagnosed and untreated disease prior to hospitalization was responsible for the development of deep-seated bacterial lesions, which were not accessible to otherwise adequate antibiotic therapy. Cardiac failure was due not only to the bacterial infection prior to treatment but to the continuing effect of the bacterial lesions that were not reached by antibiotics, despite almost a year of treatment.

1088 Park Ave. (Dr. Friedberg).

BARBERS' PILONIDAL SINUS

John Godwin Downing, M.D., Boston

A 71-year-old man, who has been a barber for 40 years, stopped work in August, 1950, because of dermatitis of the right hand. While he was cutting hair, short bristles would frequently irritate the second interspace of his right hand. Gradually, a rash appeared at this area and spread over the hand and forearm. Examination on Sept. 25, 1950, showed marked erythema, edema, and vesiculation of the fingers of both hands. The patient said he had had no eruption elsewhere. This dermatitis responded to soothing treatment in three weeks. The patient then admitted having an ulcer on his right ankle, which had not responded to treatment by a vascular surgeon, and he requested therapy. The ulcer healed on Nov. 7. His right hand had remained well; however, a small, red, pouting sinus was seen at the right second interspace. Protruding from this sinus was a small hair; in fact, the lesion looked like an infected hair follicle. This was considered unusual, inasmuch as hair follicles do not exist at the digital spaces. Noting my interest, the patient immediately squeezed the surface of the interdigital skin, and two hairs protruded. He then informed me that he was constantly extruding hairs from this opening, and, by squeezing the area, other hairs appeared.

Despite the fact that I have treated many barbers and hairdressers, this type of sinus formation was novel in my experience; however, a review of recent literature proved that Patey and Scarff [1] had described a discharging sinus at the right fourth interdigital web of a 31-year-old barber. The entire sinus was excised, and the histological appearance was said to be identical to that of a postanal pilonidal sinus, being lined with squamous epithelium and containing a hair follicle. The deeper part of the tract was lined by granulation tissue and debris. They concluded that the history of the case and difficulty of any developmental anomaly appearing at this site was strong evidence that the case was one of a pilonidal sinus, due to puncture of the skin by a hair. They stated that this type of lesion, or a type similar to it, was common among barbers and hairdressers; however, I think it must be rare in this country.

Following Patey's and Scarff's report, Ewing [2] described a painful swelling on the dorsum of the right third interdigital web of a 52-year-old barber. The swelling followed the patient's removal of hairs at this area. On examination, a thin, tender, thread-like tract could be palpated at this area, extending 1.5 cm. proximally from the sinus opening. The lesion was dissected away, and histological examination revealed a typical foreign body granuloma with giant cells. No hair, hair follicles, or squamous epithelium could be seen. Ewing was not convinced of Patey's and Scarff's theory that a small proportion of pilonidal sinuses were developmental in origin and that a great majority were of an acquired infective origin, often initiated by an ingrowing hair.

Pouting sinus containing hair.

In a later report Patey and Scarff [3] mentioned another barber who had a similar pilonidal sinus. As a result of their observations, they postulated that pilonidal sinus is not fully explained on a developmental basis but is essentially an acquired infective and foreign body reaction to buried hair. They explained the occurrence of pilonidal sinus in the fingerwebs and postanal areas as due to alternating tightening and loosening of tissue in these areas. Extensive driving on hard seats predisposes to pilonidal sinus, "jeep disease." The suction caused by the skin moving back and forth over the sacrum draws hairs into the soft tissues. This, however, does not explain the occurrence of pilonidal sinus in young women who show an absence of any but the fine lanugo hairs in this area.

520 Commonwealth Ave.

1. Patey, D. H., and Scarff, R. W.: Pathology of Postanal Pilonidal Sinus: Its Bearing on Treatment, Lancet **2**: 484, 1946.

2. Ewing, M. R.: Hair-Bearing Sinus, Letters to the Editor, Lancet **1**: 427, 1947.

3. Patey, D. H., and Scarff, R. W.: Pilonidal Sinus in a Barber's Hand, with Observations on Postnatal Pilonidal Sinus, Lancet **2**: 13, 1948.

COUNCIL ON PHARMACY AND CHEMISTRY

REPORT TO THE COUNCIL

The Council has authorized publication of the following report from its Committee on Research.

ROBERT T. STORMONT, M.D., *Secretary.*

The Committee on Research, through its Subcommittee on Steroids and Cancer, is sponsoring a collaborative study on steroids and mammary cancer. Reports summarizing this work have been published (Estrogens and Androgens in Mammary Cancer, Report to the Council on Pharmacy and Chemistry, J. A. M. A. 140:1214 [Aug. 13] 1949. Proceedings of the First Conference on Steroid Hormones and Mammary Cancer, Chicago, A. M. A. [April] 1949. Current Status of Hormone Therapy of Advanced Mammary Cancer, Report to the Council on Pharmacy and Chemistry, J. A. M. A. 146:471 [June 2] 1951).

In the following report, the conclusions expressed are those of the authors and final conclusions of the Subcommittee must await evaluation of the studies now in progress.

PAUL L. WERMER, M.D., *Secretary.*

EFFECT OF TESTOSTERONE ON PATIENTS WITH BONE METASTASES

A METABOLIC STUDY, PARTICULARLY OF BREAST CARCINOMA

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Judith Bellin, M.S., Estelle D. Gottesman, B.S.
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In the past decade, hormonal therapy has been advocated in the palliative management of patients with metastatic breast carcinoma [1]; reports of temporary palliation have been published from many centers,[2] and a wide discrepancy between the incidence of subjective and objective improvement has been noted.

In a preceding paper,[3a] it was pointed out that metabolic studies are an important aid in defining the course of malignant disease, in gaging the effect of therapeutic agents, and in studying their mode of action. The mineral metabolism of patients with active osteolysis has been characterized by elevated urinary calcium and phosphorus excretions and negative balances.[3] At times, excessive rates of demineralization exceed the ability of the kidneys to excrete calcium, resulting in hypercalcemia.[3a] Conversely, patients with osteoblastic metastases have characteristically subnormal urinary calcium excretion and a tendency to maximal calcium retention.[4] On occasion, patients with osteolytic metastases may spontaneously have temporary phases of bone repair, evidenced by a metabolic behavior that approaches the calcium-retentive traits seen in osteoblastic cases.

The purpose of the present study is to observe the effect of testosterone on the metabolism of patients with osteolytic metastases secondary to breast carcinoma. If the hormone were to encourage the remineralization of osteolytic areas, the process would be evidenced by improvement in the mineral balances.

After metabolic studies in the pretreatment phase, testosterone was administered to six patients [5] with osteolytic metastases secondary to breast carcinoma. To assess whether the results attained were specific for breast carcinoma, a tumor that is presumed to be influenced by hormones, control studies were performed with patients having other types of malignancy. A patient with extensive osteolytic metastases secondary to leiomyosarcoma of the vulva was given testosterone. A male patient with multiple myeloma was given estrogen therapy initially and later testosterone. Finally, the effect of radiation castration was observed in a premenopausal patient with osteolytic metastases secondary to breast carcinoma.

The various effects observed are illustrated by the cases reported in this paper.

NITROGEN RETENTION INDUCED BY TESTOSTERONE WITH MINIMAL IMPROVEMENT IN CALCIUM BALANCE

Case 1, a 50-year-old white woman, had extensive osteolytic and pulmonary metastases secondary to leiomyosarcoma of the vulva that had been resected three years previously. Metastases, which progressed slowly, were noted a year later. At no time during the course of the disease were major complications, such as severe anemia, pathologic fracture, or hypercalcemia, noted.

Metabolic studies were conducted for a total of 153 days (fig. 1). At that time, the patient was ambulatory and in a fairly good nutritional state. The pretreatment phase lasted for 21 days, during which the patient was in slightly positive nitrogen and phosphorus balance and in negative calcium balance with a moderately elevated urinary calcium excretion.

Upon the administration of testosterone, a total of 2.25 gm. in 45 days, urinary nitrogen excretion dropped immediately, resulting in a highly positive nitrogen balance. The calcinuria was somewhat decreased, so that the calcium balance was slightly less negative.

The studies were then discontinued for 62 days during which time testosterone was not administered. In the first 15 days after the resumption of studies, the nitrogen and phosphorus balances were similar to those observed in the first pretreatment phase, but the urinary and fecal calcium values were lower than previously. Upon the additional administration of 1.8 gm. of testosterone in 36 days, an immediate drop in urinary nitrogen and phosphorus excretion was again noted, resulting in a positive nitrogen and phosphorus balance. The calcium excretion, however, showed no further change.

To observe the possible favorable effect of testosterone on the mineral balance if an adequate supply of calcium were furnished, the daily administration of testosterone was continued in conjunction with an increased calcium intake. In this patient the presumption did not prove to be correct. Although the anabolic effect of testosterone on the nitrogen metabolism was still clearly demonstrable, the urinary calcium remained uninfluenced. The calcium balance became positive but to an extent no greater than that observed when calcium intake was increased without the additional administration of testosterone.[3a] With increased fecal calcium elimination, more phosphorus was now excreted through the stool and the phosphorus balance became somewhat less positive. These changes are similar to those seen in patients on a similar dietary calcium:phosphorus ratio who did not receive testosterone.

This case illustrates a definite anabolic effect of testosterone on protein metabolism. It induced a total retention of 194 gm. of nitrogen corresponding to 1,213 gm. of protein. The patient gained only 1.2 kg. of body weight in this phase. No major changes were noted in the patient's clinical condition and laboratory data with the exception of roentgenograms which showed slow progression of osteolysis. No major improvement of the calcium metabolism was induced by testosterone.

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MINERAL LOSS INDUCED BY TESTOSTERONE IN SPITE OF NITROGEN RETENTION

Case 2, a 57-year-old postmenopausal woman, had carcinoma of the left breast. Radical mastectomy, followed by radiotherapy, was performed and the patient was asymptomatic for four years, when extensive osteolytic metastases with spontaneous hypercalcemia developed. Testosterone was then administered but resulted only in temporary symptomatic improvement followed by progression of symptoms and findings. When admitted to the hospital, the patient was in hypercalcemic crisis. Testosterone was discontinued and intravenous fluid administration begun, resulting in a return of serum calcium and blood urea nitrogen values to normal levels, decrease in pain, and ambulation. At this time, the patient showed evidence of weight loss, masculinization, extensive osteolytic metastases with rib and vertebral fractures, diplopia, and blurred vision. The renal function, as measured by urinary concentration and urea clearance tests, was unimpaired.

Metabolic studies began two and one-half months after the discontinuation of testosterone and were conducted for nine periods totaling 54 days. The data are illustrated in figure 2. The pretreatment phase consisted of six periods, three on a low calcium intake and the next three on a higher calcium intake. In this phase, the nitrogen balance was in equilibrium. The phosphorus balances showed a retention on a low calcium intake which changed toward equilibrium on increased calcium intake. This change was mainly caused by an increase in fecal phosphorus and followed the trend which has already been described.[3a] The urinary calcium excretion was subnormal in the first three periods, indicating attempt at bone repair. In periods 4 to 6, the urinary calcium excretion tended to rise, but remained within normal limits. The calcium balance was only slightly negative on a low calcium intake. Minimal utilization (10%) of calcium gluconate was achieved in periods 4 to 6, resulting in only slight improvement of the calcium balance. The testosterone phase was clearly characterized by gradual decrease in urinary nitrogen and improvement in nitrogen balance. In contrast to the nitrogen retention was the mineral loss occurring during testosterone therapy. Hypercalcinuria occurred in the initial period of testosterone and increased progressively to excessive values accompanied by hyperphosphaturia. The excess urinary calcium and phosphorus loss approximated the ratio of these minerals in bone. The rate of mineral breakdown exceeded the urinary excretion, resulting in hypercalcemia. The calcium and phosphorus balances became progressively negative.

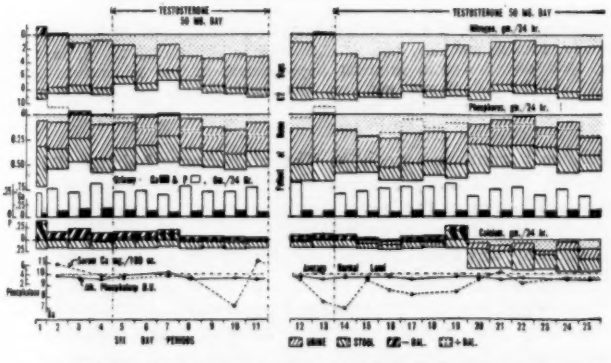

Fig. 1.—Metabolic data of a patient with leiomyosarcoma of the vulva and osteolytic metastases (case 1). All periods are for six days except periods 11 and 12 which are nine-day periods. Testosterone, 50 mg. per day, was administered in periods 5 to 11 and in periods 14 to 25, inducing nitrogen retention.

The metabolic data graph is charted according to Reifenstein, Albright, and Wells. Horizontal lines at zero in the balance graphs indicate the equilibrium between intake and output. Intake is charted from the zero line downward. Output is charted from the intake line upward toward the zero line. Interrupted lines in the phosphorus graph represent areas corresponding to the theoretical phosphorus retention or loss, calculated on the basis of theoretical N:P and Ca:P ratios. One unit of the phosphorus scale equals 15 units of the nitrogen scale and 2 units of the calcium scale.

Metabolic studies had to be discontinued for 11 days, at which time the serum calcium rose to 18.9 mg. per 100 cc. and the blood urea nitrogen to 74.8 mg. per 100 cc. Urinary collections were resumed for two periods when only intravenous feeding was feasible. Although a trend toward improvement in serum calcium and blood urea nitrogen levels was achieved, the patient died several days later of uremia. In the last period, almost 0.9 gm. of urinary calcium was excreted daily. At autopsy, marked nephrocalcinosis was found.

MINERAL AND NITROGEN LOSS INDUCED BY TESTOSTERONE

Case 3, a 47-year-old woman, underwent a left radical mastectomy two years prior to metabolic studies. Soon after the operation, osseous metastases were noted and the patient became bedridden with pain. The administration of 0.8 gm. of testosterone resulted in a cessation of menses but produced no symptomatic improvement. Subsequent radiotherapy to the lumbar spine and pelvis did not produce relief. Five months later, after a hypercalcemic crisis which improved after parenteral fluid was administered, testosterone therapy was reinstituted, the patient receiving a total of 4.1 gm. over a nine-month period. This therapy provoked hypercalcemia (15.1 mg. per 100 cc.), hypopotassemia (6.7 mg. per 100 cc.), nausea, vomiting, and dehydration. Testosterone was discontinued, and parenteral fluid and potassium were administered, resulting in a return to normal of the serum calcium and potassium within three weeks. However, anorexia and vomiting persisted, the blood urea nitrogen was 24.5 mg. per 100 cc., and the patient sustained a pathologic fracture of the left femur.

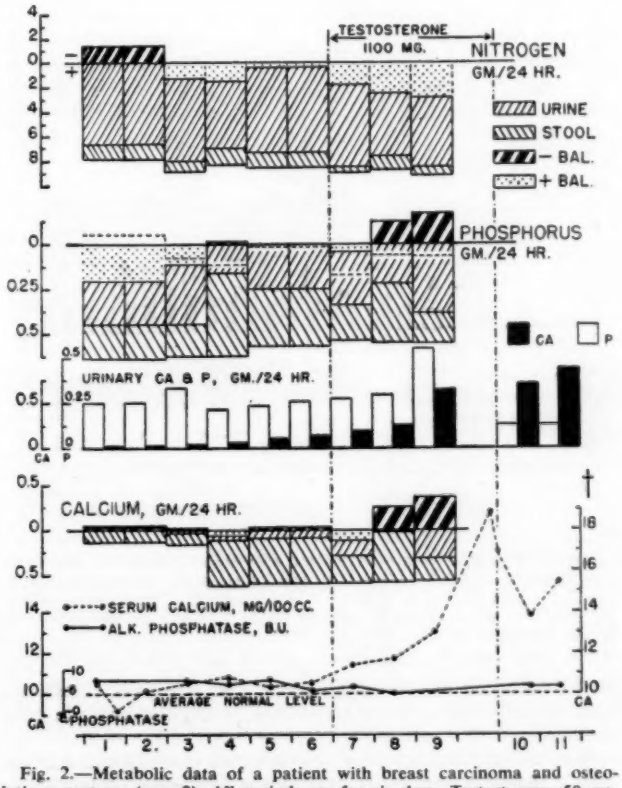

Fig. 2.—Metabolic data of a patient with breast carcinoma and osteolytic metastases (case 2). All periods are for six days. Testosterone, 50 mg. per day, was administered in periods 7 to 9, inducing hypercalcemia, nitrogen retention, and negativity of mineral balances.

Ten days later, at the time metabolic studies began, the patient had been bedridden for 22 months and was in poor nutri-

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5. These cases have been mentioned in a previous report as cases 3, 4, 6, 7, 8, and 9 (see footnote 3a). Cases 2 and 3 of this paper correspond to cases 8 and 9 of the previous report and are now described in detail as illustrative of the results obtained in this series.

tional state. The studies totaled 155 days, and are shown in figure 3. During the first five days of study, a moderately elevated calcinuria was noted. Later, urinary calcium excretion dropped toward subnormal values (as low as 20 mg. per day), calcium balance improved and was only slightly negative on a low calcium intake, and the patient was maintained in a state of nitrogen and phosphorus balance. The serum calcium was normal and the alkaline phosphatase elevated.

After 53 days of study, a total of 1.2 gm. of testosterone was administered intramuscularly in 24 days. Nine days after the institution of the hormone therapy, nausea and vomiting recurred, and the food and fluid intake decreased. Urinary calcium and phosphorus excretions rose rapidly. In the second period of hormone administration, the serum calcium rose to hypercalcemic levels and the alkaline phosphatase fell, indicating accelerated osteolysis. The average calcium balance during testosterone administration (–628) was five times that of the pretreatment periods (–129). The phosphorus balance, which was in equilibrium during the pretreatment phase, became negative because

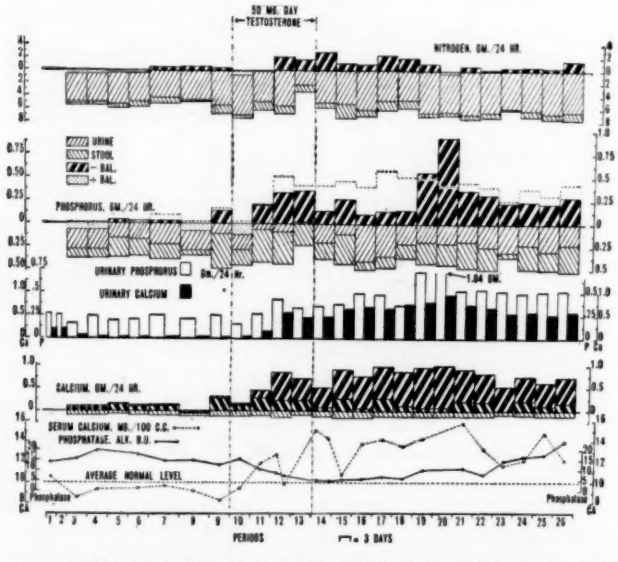

Fig. 3.—Metabolic data of a patient with breast carcinoma and osteolytic metastases (case 3). All periods are for six days except periods 1, 2, 7, and 8, which total 3, 2, 9, and 9 days respectively. Testosterone, 50 mg. per day, was administered in periods 10 to 13, inducing osteolysis and hypercalcemia.

of the increased urinary phosphorus. The nitrogen balance became negative due to nausea, vomiting, and the decrease in food intake.

With the discontinuation of testosterone, vomiting became less severe. However, the urinary calcium and phosphorus excretions increased still further, reaching a peak of 0.94 gm. and 1.043 gm. per day, respectively, six weeks after the discontinuation of testosterone. Clinically, during this phase, the patient showed a progressive downhill course. Accelerated tumor growth was evidenced by a rapidly enlarging nodular liver. Hypercalcemia, azotemia, and negative mineral balances persisted until death which occurred 12 weeks after the discontinuation of the hormonal therapy.

In summary, this case illustrates the metabolic behavior of a patient recovering from a previous hypercalcemic crisis induced by testosterone and in whom definite attempts at bone repair were observable. Reinstitution of testosterone induced another hypercalcemic crisis with excessive bone breakdown which persisted even after hormone therapy was stopped.

IMPROVEMENT IN CALCIUM BALANCE INDUCED BY DIETHYLSTILBESTROL; IMPROVEMENT IN NITROGEN BALANCE INDUCED BY TESTOSTERONE

Case 4, a 67-year-old white man, had multiple myeloma with extensive osteolysis. Ten weeks prior to the onset of metabolic studies, a compression fracture of the seventh thoracic vertebra caused paraplegia. A course of radiotherapy to the dorsal spine did not relieve pain nor did it improve the paraplegia.

Metabolic studies were performed for 288 days (fig. 4). In the four periods prior to treatment, the patient was in a state of positive nitrogen balance and of phosphorus equilibrium. The urinary calcium excretion was moderately elevated, averaging 0.212 gm. per day, and the balance was negative.

During the following 54 days, 15 mg. per day of diethylstilbestrol ("stilbestrol") was administered intramuscularly, totaling 0.81 gm. Urinary nitrogen excretion increased slightly and the

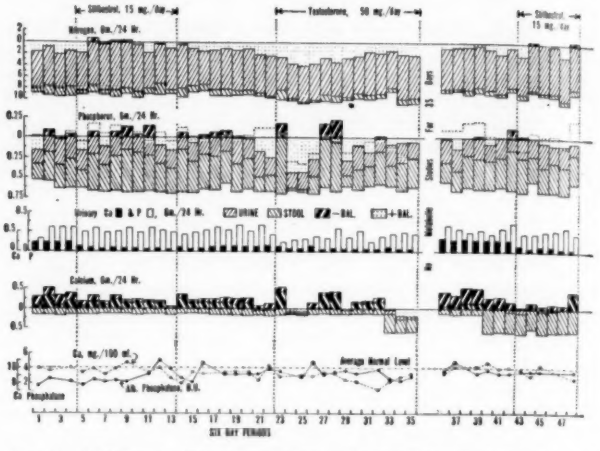

Fig. 4.—Metabolic data of a patient with multiple myeloma (case 4). All periods are for six days. Diethylstilbestrol, 15 mg. per day, was administered in periods 5 to 13 and improved the calcium balance. Testosterone, 50 mg. per day, was administered in periods 23 to 35, inducing nitrogen retention with minimal improvement in the mineral balances. Diethylstilbestrol, 15 mg. per day, was administered in periods 45 to 48 and improved the mineral balances.

balance became less positive. The phosphorus balance did not change. The urinary calcium excretion dropped promptly and reached values at the lowest limits of normal, resulting in improvement of the calcium balance.

Therapy was then discontinued during the following 54 days. The nitrogen balance returned to the previous pretreatment level. The phosphorus balance remained unchanged. Urinary calcium excretion rose slightly and the balance was slightly more negative.

For the following 60 days 50 mg. of testosterone was administered daily, totaling 3 gm. Urinary nitrogen excretion decreased promptly, greatly improving the nitrogen balance. Urinary calcium and phosphorus decreased slightly, resulting in minimal improvement of the mineral balance.

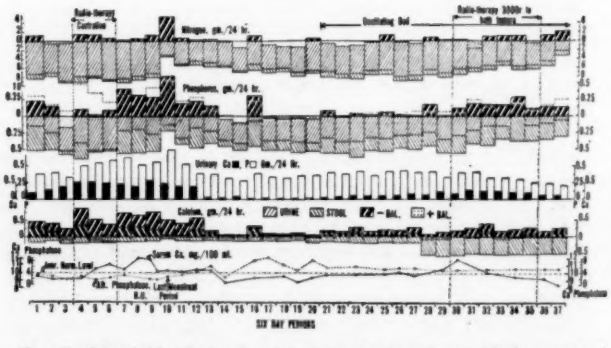

Fig. 5.—Metabolic data of a premenopausal patient with breast carcinoma (case 5). All periods are for six days except period 1, which was for nine days. Radiation castration induced an artificial menopause with improvement in the mineral balances. Subsequent radiotherapy to osteolytic areas in both femora achieved minimal improvement in the calcium balance.

In the succeeding 18 days of study, calcium gluconate was administered orally to increase the calcium intake, and testosterone administration was continued. The urinary nitrogen increased slightly, resulting in a somewhat less positive nitrogen balance. The phosphorus balance did not change significantly. The urinary calcium excretion did not change. However, ap-

proximately 80% of the increased calcium intake was retained, resulting in a reversal to positive calcium balance.

Studies were interrupted for 35 days, during which time no hormone was administered. Upon resumption of studies in period 36, the patient was found to have elevated urinary calcium excretion (0.281 gm. per day) and negative calcium balance, with the nitrogen and phosphorus approximately in balance. The oral administration of calcium gluconate did not change the calcinuria but improved the calcium balance with 45% utilization of the added calcium. When diethylstilbestrol was again administered, 0.54 gm. in 36 days, together with calcium gluconate, urinary calcium values decreased, calcium balance further improved, and utilization of the added calcium was 67%. As in the previous course of diethylstilbestrol therapy, the nitrogen excretion rose and the balance was less positive.

In summary, the data illustrate the metabolic behavior of a patient with advanced multiple myeloma and marked osteolysis. Diethylstilbestrol administration improved the calcium balance but only slightly affected nitrogen and phosphorus metabolism. Administration of testosterone improved nitrogen retention but had only minimal effect on calcium and phosphorus metabolism. However, supplementation of the calcium intake resulted in a high rate of utilization of the added calcium. After the effect of hormonal therapy had subsided, mineral catabolism was again evident. Subsequent administration of diethylstilbestrol was shown to achieve the same mineral anabolic effects as were obtained previously.

IMPROVEMENT IN MINERAL BALANCE INDUCED BY RADIATION CASTRATION

Case 5, a 38-year-old white woman, had extensive osteolytic metastases secondary to breast carcinoma. A radical mastectomy followed by radiotherapy was performed. Osteolytic metastases were noted one year later and the patient was admitted to the metabolic ward for further study.

Metabolic studies were performed for 225 days (fig. 5). The course of the patient can be divided into three distinct phases: (1) osteolytic crisis before castration (periods 1 to 13), (2) beneficial effects of castration with metabolic data suggestive of bone repair, and (3) recurrence of osteolytic activity.

In the first phase, excessive bone breakdown is clearly evidenced by high and continuously increasing urinary calcium and phosphorus excretion and a progressively more negative mineral balance. During period 9, the urinary calcium and phosphorus excretion reached a peak, with negative mineral balances. The excretion of calcium and phosphorus did not keep pace with the rapid rate of bone breakdown, resulting in hypercalcemia and hyperphosphatemia.

After 21 days of observation, radiotherapy was administered to achieve castration, 1,000 r to three pelvic portals. The patient's last menstrual period occurred in period 10. In period 13, 36 days after the completion of radiotherapy, a sudden improvement in the mineral balance occurred. The urinary calcium excretion dropped from 397 to 56 mg. per day, and progressively declined to subnormal levels. The calcium balance improved and became only slightly negative, as is normal with a low calcium intake. The nitrogen and phosphorus balance also improved. The attempt at bone repair is evidenced by a subnormal urinary calcium, a calcium balance approximating equilibrium even on a low calcium intake, and by rising serum alkaline phosphatase values.

This second phase, in which the patient experienced the greatest beneficial effect of castration, lasted 66 days. The urinary calcium and phosphorus excretion then increased progressively. The mineral balance became more negative, indicating renewed bone breakdown. In an attempt to improve the patient's calcium retention, she was placed on an oscillating bed and her low calcium diet was supplemented with calcium gluconate given orally. However, utilization of the supplemented calcium was only 21%, the urinary calcium continued to rise, and the calcium balance remained negative, despite the higher intake.

Because of the danger of pathologic fractures, radiotherapy, 3,000 r to both femora, was administered during periods 31 to 36. The urinary calcium and phosphorus continued to rise until period 35 and then began to fall slightly. Upon the completion of radiotherapy, the urinary mineral excretion improved still further, although the patient was still in negative calcium balance, even on a high calcium intake. It is to be noted that this second phase of osteolysis, occurring after castration, was not as severe as the osteolytic crisis seen while the patient was still menstruating.

In summary, this case illustrates the improvement in mineral metabolism upon radiation castration of a patient in an osteolytic crisis. This favorable effect, however, was only temporary, and further bone breakdown could not be prevented even with the aid of an oscillating bed and a higher calcium intake. Subsequent local radiotherapy at the beginning of a second osteolytic phase may have prevented, for a time, further excessive bone breakdown.

DISCUSSION

To observe some effects of malignancy on metabolism and evaluate the action of therapeutic agents, 42 patients were studied in the metabolic ward. Of this group, 24 patients had extensive osteolytic malignancy, 8 had osteoblastic metastases, 5 cancer patients had no bone metastases, and 5 patients had nonmalignant disease. Five cases in this series are reported here to illustrate certain points.

Previous reports [3] have presented data which show that active osteolysis secondary to malignancy is characterized by hypercalcinuria, hyperphosphaturia, and negative mineral balances. In cases of extremely rapid bone destruction, these metabolic trends are accentuated, the ability of the kidneys to excrete calcium is exceeded, and hypercalcemia results.[3a] It has been demonstrated [3a] that the mineral catabolism of osteolytic metastases is not specific for any one type of malignancy but is characteristic for all malignancies that cause bone destruction. Metabolic evidence has been presented showing that even advanced malignancy is characterized by periods of spontaneous remissions and exacerbations.[3a]

In bone metastases that cause an osteoblastic response, the metabolism is characterized by extremely low urinary calcium excretion and a calcium balance more positive than normal.[4] Data from this study indicate that improvement in osteolytic metastases is manifested by calcium and phosphorus metabolism that approaches normal and, with rapid bone repair, will even approximate the extreme calcium retention seen in osteoblastic cases.

The present study was conducted to evaluate the effect of hormonal therapy in patients with osteolytic metastases. In assessing the results obtained, an attempt will be made to differentiate between specific effect of the hormone on tumor and nonspecific effect on demineralizing bone. Previous metabolic studies have defined some factors that influence osteogenesis. The skeletal system of normal adults is in a dynamic equilibrium of resorption balanced by an equal rate of new bone formation.[6]

Some of the factors influencing osteogenesis are: (1) dietary intake of the building blocks of bone, (2) absorption from the intestinal tract into the blood stream, (3) utilization of the building blocks by the bone influenced by such endocrine factors as pituitary growth hormone,[7a] gonadal,[8] thyroid,[9] parathyroid,[10] and adrenocortical hormones,[7] (4) functional use of the skeleton,[11] and (5) excretion of minerals.[12]

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Impairment of any of these factors can cause osteolytic bone disease characterized metabolically by hypercalcinuria, hyperphosphaturia, and negative mineral balances, similar to the data obtained in osteolytic malignancies. Metabolic studies have been reported for osteomalacia,[12] steatorrhea,[13] postmenopausal and senile osteoporosis,[14] hyperparathyroidism,[10] Cushing's disease,[13b] immobilization,[11] and renal rickets.[12]

In a number of these diseases, particularly in postmenopausal osteoporosis, androgen and estrogen therapy has induced improvement in calcium, phosphorus, and nitrogen metabolism.[14b] It has been noted that androgen has a significant protein anabolic effect, whereas estrogen induces predominantly mineral anabolism.

In patients with malignant bone disease, severe pain may cause immobilization, and osteoporosis from disuse is often a prominent feature. When gonadal hormones are administered to these patients, a favorable effect may be achieved on the osteoporosis, one that may be entirely nonspecific with respect to tumor growth.

For the purpose of this discussion, a specific effect on tumor shall be considered as one that causes inhibition or acceleration of tumor growth.

Experimental evidence has been advanced indicating that the incidence of mammary carcinoma in susceptible strains of mice is influenced by hormonal factors. This subject has been recently reviewed.[15] It has been demonstrated that ovariectomy decreased the incidence and delayed the appearance of mammary carcinoma in female mice of a susceptible strain [16]; similar results have been achieved by implantation of testes,[17] administration of testosterone,[18] and ovarian irradiation.[19] Ovarian grafts induced mammary cancer in castrated male mice of a susceptible strain and the incidence approximated that in females of that strain [20]; similar results have been achieved by administration of estrogen.[21] However, it must be stressed that these results are attained in mice of high mammary cancer strains. Androgens and estrogens apparently have no effect on the growth of a mammary tumor once it is established in a mouse.[15a]

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Numerous clinical investigations have been conducted on the therapeutic effect of hormones in human breast cancer. Surgical or x-ray castration has resulted in clinical improvement of 20 to 56% of premenopausal women with breast carcinoma.[22] Castration has also resulted in improvement of some male patients with breast cancer.[23] Haddow and his collaborators reported great improvement in patients with advanced breast cancer receiving estrogen therapy, and serial biopsies of a few patients showed histological alterations suggesting regression of tumor cells.[1a]

The Committee on Research of the American Medical Association has undertaken to assemble the data of its cooperating investigators on the effects of steroid hormones in the treatment of breast cancer.[24] In a total of 285 patients with metastases treated with androgen, subjective improvement was noted in 62%. Objective improvement in soft tissue lesions was noted in about 20%. Objective improvement in osseous lesions was reported in 18%. In a total of 144 patients treated with estrogen, subjective improvement was reported in 60%. Objective improvement in soft tissue lesions was noted in 43%; a number of osseous lesions showed improvement.

However, there have also been clinical reports suggesting tumor promotion by hormones. Cancer of the breast has appeared in male [25] and female [26] patients receiving estrogens. Apparent acceleration of tumor growth was noted in patients with metastatic breast cancer receiving estrogen or androgen therapy.[27]

Case 1 is a study of the effect of testosterone in a patient with extensive osteolytic metastases secondary to leiomyosarcoma of the vulva. The androgen induced retention of protein and had a slight mineral-anabolic effect. Since this effect is similar to the one expected in a patient with postmenopausal osteoporosis, and since leiomyosarcoma is assumed to be a tumor that is not controlled by hormones, it may be assumed that the favorable effect of testosterone in this case is not a specific tumor-inhibiting effect.

Case 2 is a study of testosterone therapy in a postmenopausal patient with extensive osteolytic metastases secondary to breast carcinoma. Testosterone had the seemingly paradoxical effect of inducing nitrogen retention together with mineral loss causing hypercalcemia. If it were assumed that testosterone induced protein anabolism in tumor tissue, the accelerated rate of tumor growth in the osseous metastases would account for the increased bone breakdown.

Case 3 is a study of the effect of testosterone in a postmenopausal patient with osteolytic metastases secondary to breast carcinoma. The pretreatment phase illustrates a trend toward spontaneous bone repair in a patient with advanced malignancy. This favorable phase was interrupted by the administration of testosterone which promptly induced accelerated osteolysis and hypercalcemia. The accompanying protein catabolism was due to anorexia; the decreased food intake, nausea, and vomiting resulted from hypercalcemia. These catabolic factors outweighed whatever protein-anabolic effect the androgen might have had. As in the previous case, the osteolysis may have been caused by a tumor-promoting effect of testosterone. However, it must also be considered that the hormone may have had a direct mineral-catabolic effect as reported in mice by Gardner and Pfeiffer.[8]

Case 4 is a study of the effects of estrogen, and later androgen, in a patient with multiple myeloma. Estrogen induced mineral anabolism, but did not improve the nitrogen balance. Androgen promoted protein retention, but improved the calcium balance only slightly. This patient was paraplegic and bedridden at the onset of studies and considerable mineral catabolism could be attributable to osteoporosis of disuse. Since multiple myeloma is not considered to be a tumor that is hormonally controlled, the beneficial effects of hormone therapy cannot be considered to be due to tumor inhibition. As in case 1, the favorable effect achieved may not be assumed to be specific for tumor, but rather one of remineralization of osteoporotic areas.

It was reported previously [3a] that 30 to 40% of the ingested calcium gluconate was utilized in patients with osteolytic breast cancer metastases, a rate similar to that observed in normal persons.[28] In case 4, when calcium gluconate was administered

with testosterone, the rate of utilization was 80%, indicating the anabolic effect of testosterone. Tracer studies with radioactive calcium and phosphorus are planned to further elucidate this point.

Case 5 is a study of the effect of radiation castration in a premenopausal patient with extensive osteolytic metastases secondary to breast carcinoma. This artificial menopause induced a definite, but temporary, improvement in mineral and protein balance. It is likely that the palliation achieved was due to tumor inhibition caused by castration.

In none of the six patients with breast cancer who received testosterone during metabolic studies was a beneficial therapeutic effect achieved. Testosterone accelerated osteolysis and induced hypercalcemia in three cases. This small series cannot be used for a statistical evaluation of the efficacy of testosterone therapy. Since the purpose of the study was to define the mechanism when testosterone had an unfavorable action, four of the cases selected for study had previously had adverse effects from androgen therapy. Statistics have been submitted from other centers on the beneficial clinical effects of testosterone.[24]

From the data presented, it appears that testosterone therapy of advanced breast cancer may be most beneficial to those patients in whom it slows down tumor growth and induces recalcification of demineralized areas. A favorable response may also be expected from patients in whom the hormone improves the osteoporosis but does not affect the tumor. However, clinical and metabolic evidence is available to indicate that androgen or estrogen may accelerate tumor growth. In these instances, a more rapid downhill course may result from hormonal administration, with pain, anemia, hypercalcemia, tendency to fracture, and accelerated growth of metastases. There does not appear to be any specific criteria that will enable prediction of the therapeutic response to testosterone in a given patient with breast cancer. Therefore, precaution in the administration of hormonal therapy is indicated, with close clinical and laboratory follow-up.

SUMMARY

1. To study the action of testosterone under controlled conditions, metabolic experiments were performed in six patients with breast cancer with osteolytic metastases.

2. Control studies were also performed in three patients with extensive osteolytic malignancy. Testosterone was administered to a patient with leiomyosarcoma. Diethylstilbestrol, and later testosterone, was administered to a patient with multiple myeloma. A premenopausal breast cancer patient received x-ray castration.

3. Testosterone induced accelerated osteolysis and hypercalcemia in three patients with breast cancer.

4. Testosterone induced nitrogen retention in the patient with leiomyosarcoma, with minimal improvement in calcium balance.

5. Diethylstilbestrol improved the mineral balance of the patient with multiple myeloma. Testosterone induced nitrogen retention, with slight improvement of the mineral balance.

6. X-ray castration of the patient with breast cancer temporarily improved the mineral balance.

7. The mechanism of these favorable and unfavorable responses to alteration in the hormonal balance has been discussed.

Patient-Physician Relationship.—The essential ingredient of a lasting patient-physician relationship is time, time skilfully apportioned so that the garrulous are not allowed more nor the inarticulate allotted less. When we begin to hurry our patients the bond that is normally strengthened through listening and understanding is weakened. And when we introduce production line methods we are no longer physicians, just licensed pill-peddlers.

The sick sense being hurried and resent it. More than anything else they want us to grant them the warm sympathetic hearing they deserve. Denied this, they search elsewhere, anywhere, for an attentive ear.

To trim time solely to see more patients per day is to develop in the direction of greater mechanical efficiency and lesser diagnostic proficiency and the net result is that patient satisfaction shrinks as time spent is reduced.—W. S. Reveno, ℞ Time, q. s., *Detroit Medical News*, March 17, 1952.

COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION

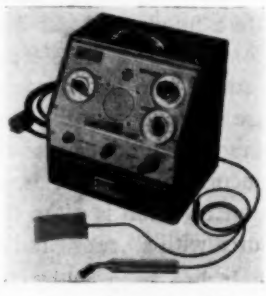
The Council on Physical Medicine and Rehabilitation has authorized publication of the following reports.

RALPH E. DE FOREST, M.D., *Secretary.*

SANBORN ELECTROPHRENIC RESPIRATOR ACCEPTED

Manufacturer: Sanborn Company, 39 Osborn St., Cambridge 39, Mass.

The Sanborn Electrophrenic Respirator is a generator of electric currents designed to stimulate the phrenic nerves and thus induce contractions of the diaphragm in apneic patients. It operates by connection with a source of 60-cycle alternating current at 115 volts. It is provided with a dispersive electrode which is applied to the patient's back and an active electrode which must be applied with pressure over the phrenic nerve in the neck. The electrical apparatus is housed in a portable case weighing 5.5 kg. (12 lb.) and measuring 25 by 24 by 20 cm. (10 by 9½ by 8 in.). Packed for shipping it measures 30.5 by 38 by 38 cm. (12 by 15 by 15 in.) and weighs 6.8 kg. (15 lb.). The foreign shipping weight is 15.9 kg.



Sanborn Electrophrenic Respirator

Evidence from sources acceptable to the Council indicated that even submaximal stimulation of one phrenic nerve by this device could provide adequate pulmonary ventilation, and that in the hands of properly trained persons under the supervision of a physician, especially under hospital conditions, the device was a means of supplying artificial respiration. Although the Council recognized the existence of certain difficulties in application of the method, the apparatus itself was found to be technically sound.

The Council on Physical Medicine and Rehabilitation voted to include the Sanborn Electrophrenic Respirator in its list of accepted devices with the express understanding that it should not be used for first aid by lay groups (such as fire departments) nor for the prolonged care of apneic patients, but that it is a satisfactory means of resuscitation when used under the direct supervision of a physician.

HEALTH RESORT FACILITIES OF WHITE SULPHUR COMPANY OF SHARON SPRINGS ACCEPTED

Operating Agency: White Sulphur Company of Sharon Springs, N. Y., Inc., Sharon Springs, N. Y.

The White Sulphur Company of Sharon Springs, N. Y., Inc., operates an extensive system of bathing establishments in Schoharie County. The distinctive natural resources is a mineral water containing a relatively high percentage of hydrogen sulfide. The management considers this institution essentially as a bathing establishment, there being no hospital connected with it. There is no laboratory and no roentgen ray department, and the physical therapy includes primarily baths, Scotch douches, and massages. Recreational facilities are offered both by the institution itself and by the community in cooperation with the institution.

The Council obtained evidence that the medical supervision was adequate and that the baths were not being exploited by cultists. Most of the patrons come without any desire for medical attention and without any expectation that the baths will give anything more than an enhanced feeling of well-being. The waters are not being promoted with therapeutic claims. The Council on Physical Medicine and Rehabilitation voted to include the Health Resort Facilities of the White Sulphur Company of Sharon Springs, N. Y., Inc., in its list of accepted health resorts.

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RADIOGRAPHY WITH RADIOACTIVE ISOTOPES

Although the influence of nuclear physics on diagnostic radiology to date has been comparatively slight, there are a number of interesting possibilities in this respect. Some of these are discussed in a recent article by Mayneord [1] who had suggested that it might be possible to use a strong radioactive source placed inside the body as a radiographic focus so that more satisfactory views from unconventional angles might be obtained. In such instances detail is often obscured by superimposed structures with standard radiographic techniques.

It has been widely assumed that the gamma rays emitted from an atomic nucleus are very penetrating and thus would not provide the contrast necessary in human radiography. Actually, a number of radioactive substances emit gamma rays of low average energy that are within the diagnostic range. Many of these radioactive substances, however, are not adaptable to diagnostic radiography. They may emit other gamma rays of higher penetration or beta rays of high energy. Other factors precluding their use may be a short life or lack of availability in sufficient quantity.

Mayneord chose thulium 170, one of several more suitable sources of gamma rays with low energy, to study its possible applications in medicine. Thulium 170 emits gamma rays having an average energy the equivalent of 0.084 mev. and also emits beta rays. The beta particles disintegrate, so that the radiation coming from thulium 170 consists of a mixture of gamma rays of 0.084 mev., characteristic x-rays of ytterbium with energies in the region of 0.050 mev., and a small fraction of penetrating rays. Thulium 170 is produced by placing thulium, a rare earth of atomic weight 169 in the pile and irradiating with slow neutrons. Thulium picks up a neutron to form thulium 170. The high cost of thulium is offset by the advantages of a source with a virtually infinite life, since it can be reactivated in the pile. The material is prepared as small flat disks, which are then irradiated.

For preliminary experiments a device was used consisting of a sphere of "perspex" plastic 1 cm. in diameter at the center of which lies a small radiation source on the end of a rod. The "perspex" sphere cuts down the formation of secondary penetrating x-rays, which must be avoided because they give a high dosage to tissues near the source and cause a loss of contrast in the roentgenograms. Thulium 170 as used in these experiments is a feeble radioactive source, and the exposures have been long, e. g., 10 or 12 hours for a source-film distance of 12 cm., although screens reduce the exposure to one hour. Roentgenograms of limited areas have been taken with exposures of only five minutes.

The first experiments were done with a dried skull. Excellent pictures of the teeth were obtained. The gaps between the teeth were clearly shown, since the rays fall orthogonally to the mandible. A number of teeth may be included in a single exposure, without obscuring of the view by the opposite mandible and with only minimal superimposition by the adjacent teeth. Photographs of parts of limbs were also obtained with the use of short focal distances.

The use of radioactive isotopes appears unlikely to compete seriously with standard radiographic techniques, because large amounts of the isotope are required; however, the advantages of such a radioactive source are independence from sources of electricity, avoidance of complex equipment, and compactness. Also, sources of greater strength and higher concentration should be available in the future from piles of high neutron flux.

Another possible use for this kind of low energy radiator is the construction of a device consisting of a Geiger counter with an arm attached holding a small source of a radioactive isotope. In this way a probing beam of radiation is obtained that may be used in localizing foreign bodies and in attempts to outline body organs, based on differential absorption of the radiation. By this method metallic foreign bodies 1 to 2 mm. in diameter were located in a wax phantom.

Preliminary observations suggest that if sources of sufficient strength can be obtained radioactive isotopes emitting gamma rays of low energy will be useful in diagnostic radiology.

1. Mayneord, W. V.: Radiography of the Human Body with Radioactive Isotopes, Lancet **1**: 276, 1952.

THE FUTURE OF OTOLARYNGOLOGY

For a number of years otolaryngology has been referred to as a shrinking surgical specialty, subject to encroachment, modification, and erosion from various sources. During the past decade chemotherapy and the antibiotics have convincingly reduced both the incidence and the need for surgical intervention in such diseases as mastoiditis, otogenic and rhinogenic intracranial complications, and infections of the neck. Acute surgical mastoiditis, for example, is so unusual today that many teaching institutions find it difficult to train novitiate otolaryngologists in the technique of a simple mastoid operation.

The conventional field of otolaryngology no longer exists as the uncontested domain of the otolaryngologist.

It is common knowledge that more tonsillectomies are done by general surgeons, physicians, and pediatricians than by otolaryngologists. A questionnaire sent by Lierle [1] to 574 general practitioners in Iowa indicated that from 1½% to 80% of their work was in the field of otolaryngology, with an average of approximately 22% of all patients seen during the months September to June. The development of thoracic surgery has restricted the otolaryngological field still further, especially since the thoracic surgeon has found it necessary to include the bronchoscope among his diagnostic and therapeutic tools. Add to this the competition supplied by the allergist, the plastic surgeon, the faciomaxillary surgeon, the roentgenologist, and the psychiatrist, and the dilemma of the present day otolaryngologist becomes fairly clear.

In 1948 Richards [2] summarized the results of a questionnaire sent to 500 members of the American Academy of Ophthalmology and Otolaryngology, the majority of whom lived in smaller cities and towns of uniform geographical distribution. To these men the future looked dim. Eighty-six per cent of the members stated they believed the field of otolaryngology to be shrinking, and nearly all of them attributed the decline to chemotherapy. In addition, reasons for the decline, either alone or as part of a number of contributing factors, were attributed to the general practitioner in 66% of the replies, to the thoracic surgeon in 50%, to the allergist in 66%, to the radiologist in 33%, and to the plastic surgeon in 66%.

In the face of these gloomy forecasts, some otolaryngologists have protested and declared that on the contrary the prospects for otolaryngology were never brighter.[3] In this connection, Richards asserts that there are two major subdivisions of the otolaryngological specialty, one the science, the other the practice. Ideally, science and practice should be combined as an integrated unit; practically they are often widely separated. Considering the purely scientific aspects of the problem, it is generally agreed that the future of otolaryngological research, investigation, and hence the potentialities for new discoveries, is limitless. Most experimentation can be carried on only in teaching institutions and hospital laboratories furnished with adequate equipment, manned by investigators with exceptional interest and skill, and supported by generous endowments and grants-in-aid. Given these factors, the future of scientific otolaryngology seems assured. But for the physician who enters the practice of otolaryngology as a principal, if not sole, means of livelihood, the constrictions and encroachments on the specialty are matters of immediate import.

To meet the challenge, various measures have been suggested. It has been proposed that the future otolaryngologist expand the sphere of his activities to include not only conventional diseases of the ear, nose, and throat, but surgery of the neck and thyroid gland, reconstructive surgery of the head and neck, bronchoesophagology, allergy, audiology, and physical medicine.[4] More otolaryngologists are urged to become qualified to deal with surgical treatment of cancer of the larynx.[5] In some quarters, it is maintained that the well-rounded, adequately prepared otolaryngologist should be a composite paragon, trained as an anatomist, a physiologist, a biochemist, an audiophysicist, an allergist, internist, radiologist, surgeon, and even psychiatrist. At present, declares Richards, this is hardly a feasible solution to the otolaryngologist's dilemma. The training required would entail so prolonged a preparation as to be far beyond the time and money available to most physicians.

Whether, as has been proclaimed, "the future of otolaryngology was never brighter than at present,"[3] or "otolaryngology may be in a dilemma but the future is not dark,"[1] or "the good old days of otolaryngology are gone forever," it is axiomatic that only in a climate of continuously free and open discussion can a valid, objective assessment of the future of otolaryngology be made. Otolaryngologists have much to gain by thrashing out the problem calmly and deliberately rather than by ignoring it.

THE LARGEST MEDICAL EXHIBIT

Visitors to the annual session of the American Medical Association in Chicago, June 9-13, will be privileged to see what is believed to be the world's largest and most comprehensive medical exhibit. In addition to 300 scientific exhibits portraying recent advances in clinical and laboratory medicine, there will be 375 technical exhibits displaying new drugs, instruments, books, and services of interest to physicians. The regular scientific exhibits, covering almost every branch of medicine, will be supplemented by special demonstrations on resuscitation, fresh pathological specimens, and treatment of fractures, as well as by exhibit symposiums on diabetes, overweight, and cardiovascular disease. The technical exhibits will be staffed by qualified personnel who will discuss the diagnostic and therapeutic uses of the products demonstrated. Together the scientific and technical exhibits will occupy nearly a quarter of a million square feet of floor space on Chicago's Navy Pier and will have a frontage of more than three miles. Thousands of physicians and other medical personnel and guests from all parts of the country are expected to visit these exhibits. Many have already made hotel reservations. For those who have not yet done so, an application blank is provided on page 75 of the advertising section in this issue of THE JOURNAL. All physicians planning to attend are urged to make their reservations at the earliest possible date to avoid last-minute disappointment.

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1. Lierle, D. M.: The Present Status and the Future of Otolaryngology, Ann. Otol. Rhin. & Laryng. **59**: 496 (June) 1950.
2. Richards, L. G.: Otolaryngology in Transition: Presidential Address, Laryngoscope **58**: 455 (June) 1948.
3. Johnston, W. H.: Modern Trends of Surgery and Treatment in Otolaryngology, J. A. M. A. **144**: 977 (Nov. 18) 1950.
4. Lederer, F. L.: The Broadened Scope of Otolaryngology, J. Internat. Coll. Surgeons **13**: 597 (May) 1950.
5. McCart, H.: The Future of Our Specialty, Laryngoscope **59**: 417 (April) 1949.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

The economics of medicine, which for generations involved little more than a patient's payment of money or goods to the physician in return for medical service, has become a complex science. Development of hospitals, group practice, specialization, ancillary services, new drugs and devices, sickness insurance, and modern transportation have all contributed to its complexity. The modern practitioner not only must be a student of medicine but must be grounded in economics and sociology as well.

To aid physicians in understanding the socioeconomic side of medicine, your A. M. A. in 1931 created a Bureau of Medical Economic Research. Since 1946 it has been under the able direction of Frank G. Dickinson, Ph. D., who taught economics at the University of Illinois for 25 years. Its purpose is to study all phases of economics pertaining to the practice of medicine and report its findings to the profession. It operates in an atmosphere of academic freedom. The A. M. A. wants unbiased facts. The Bureau presents these and attempts to throw them against the screen of the total economic picture so that they appear in true perspective. Any action taken by the A. M. A. based on these findings is the decision of the House of Delegates, which is the policy making body. In the course of uncovering medical economic data, the Bureau has repeatedly exploded statistical myths. Some of these had long been favorites of the advocates of state medicine for "illustrating" the shortcomings of our free system of medical care. In this respect the Bureau has provided us with powerful ammunition in our battle against socialization.

An outstanding example may be found in the study of the supply and distribution of physicians in the United States. The commonest yardstick in use up until a few years ago was the number of physicians in relation to population by counties. Voices were frequently raised to lament the fact that many counties had few or no physicians. To our economists this was absurd. It ignored the fact that some counties had only a handful of residents. It further ignored the obvious fact that persons cross county lines to seek medical care just as they do to buy groceries. A "doctorless" county might have three or four easily accessible, well-staffed hospitals located just inside the neighboring counties.

In order to ascertain the facts about physican supply and distribution, the Bureau has divided the country into 757 medical service areas based on knowledge concerning where persons go for their medical care. These areas roughly correspond to the trading areas used by students of consumer buying habits. By determining the number of physicians in relation to population in these areas, we can see where shortages and surpluses actually occur. This study, which will be completed in the fall after more than three years' work, will be invaluable to placement services in advising young physicians where to settle. Communities in areas shown to be short of physicians can be encouraged to take steps to attract physicians. Research already completed reveals, however, that the U. S. has an amazingly adequate distribution of physicians. It has laid forever the ghost of many so-called doctorless counties.

Other studies of the Bureau of Medical Economic Research that are of great interest to the profession are the recent survey of physicians' incomes, conducted jointly with the U. S. Department of Commerce, and a study just completed of health services in universities. The former helped to "scotch" rumors that all doctors are in the upper income brackets. It revealed that physicians engaged in civilian practice in 1949 had an average income of $11,058 before taxes. In the 20 year period since 1929 the average income of physicians had more than doubled, but the increase was practically identical with that for all earners in the general population over the same period.

The recent survey of university health services discloses that most schools provide such service for students. Large schools employ full-time physicians. Faculty members and other employees, however, are generally regarded as citizens of the community, and, as such, they obtain medical care from private physicians.

Group practice has been of continuing interest to the Bureau. It has just published a bibliography on the subject, Bulletin 85, which lists all pertinent articles written during the last 20 years. In addition, it has in preparation a discussion of the number of group practices that were dissolved during the 1940's and the reason for the termination.

Maternal and infant mortality, life expectancy, leading causes of death, and other statistical data that point up medicine's success or failure in its battle against disease also concern the Bureau. It uncovered the fact that accidents are the leading cause of death when measured in terms of working years lost. This information has been used widely by the National Safety Council.

One of the most important functions of the Bureau is its continuing inquiry into the cost of medical care. This it relates to fluctuations in the cost of living and the prices of other commodities that the wage-earner must purchase.

How does the Bureau uncover its facts? It carefully analyzes and makes use of data developed by agencies of the federal and state governments and by private research organizations. Original surveys are conducted by mailed questionnaires. The Bureau maintains the only IBM installation at A. M. A. headquarters, and it is used primarily for such research projects. Eventually, punch cards containing a wide variety of statistical data on all physicians will be available for these studies.

Through its statistical experts and its IBM installation, the Bureau performs many valuable services for other departments of the Association. It designed and conducted a national survey of blood banks for the A. M. A. committee working in that field. It compiles the statistics for the annual hospital and internship and residency numbers of THE JOURNAL. This is done to assist the Council on Medical Education and Hospitals. The Bureau has aided the Public Relations Department in the compilation of results of public opinion surveys.

While the Bureau publications are, of necessity, rather heavy reading, they contain enlightening facts and exciting discoveries for the student of medical economics. A catalog may be obtained by writing to the Bureau of Medical Economic Research. I commend these bulletins most heartily to every physician, but especially to those who guide medicine's progress in socioeconomic fields. For the leaders of state and county medical associations, for physicians active in health insurance programs, and for the increasing number of teachers of economics in our medical schools, these Bureau bulletins are extremely valuable.

There are those who would steer medicine's ship into the treacherous waters of a socialist economy. The rocks of regimentation and the sand bars of impractical "welfare" schemes are on all sides. It is not enough that we have a steady hand on the rudder. We must also operate on the basis of fact and clear economic understanding in order that the course of medicine in a changing world will endanger neither its quality nor its freedom.

JOHN W. CLINE, M.D., San Francisco.

ORGANIZATION SECTION

FEDERAL MEDICAL LEGISLATION

Deductions from Income for Retirement

Representative Coudert of New York introduced H. R. 7426 to provide that certain amounts expended by individuals for the purchase of non-interest-bearing United States bonds may be deducted in computing net income. This bill would enable taxpayers to lay aside savings during more productive years for disability and retirement eventualities. Taxpayers would be permitted to purchase United States bonds up to 10% of their adjusted gross income. Bonds would be non-interest-bearing, have no fixed maturity, be payable in full on demand, and would be issued only to individuals. The proceeds received by the U. S. from the sale of these special bonds would be used to retire outstanding, high interest-bearing bonds. A deduction from income would be permitted during the years in which bonds were purchased, but the proceeds would be taxable when sold by the individual on the same basis as any other income. If the individual should die, proceeds would be included in his gross estate. Representative Coudert previously introduced in this Congress two other bills to accomplish the same purposes, H. R. 3456 and H. R. 5847. The first bill provided for postponement of federal income taxes for a limited portion of income, which could be contributed to a restricted retirement fund. The second bill would allow income tax deduction for premiums paid on life insurance and annuity contracts.

Air Pollution

H. Res. 593, introduced by Representative Dollinger of New York, proposes the creation of a select committee composed of seven members of the House of Representatives to conduct a full and complete investigation and study of air pollution in the United States. The committee would be expected to suggest effective methods of eliminating or controlling air pollution. None of six similar measures, previously reported, called for the appointment of a special committee made up of the members of Congress.

STATE MEDICAL LEGISLATION

Arizona

Bill Enacted.—S.C.R. 11, was adopted March 20, 1952. It provides for submission to the people of a measure providing for the creation by the legislature of a **department of public health or welfare** to consist of the commissioner of public health and welfare, the board of public health and welfare, the divisions of the department, and such other boards, councils and institutions or agencies as the legislature may deem necessary or advisable.

California

Bills Enacted.—S.R. 34, was adopted April 1, 1952. It provides for the creation of an Interim Commission to ascertain, study and analyze all facts relating to **all state hospitals and veterans' institutions** whatever their nature.

Michigan

Bills Enacted.—H. 202, has become Public Act No. 93 of the Acts of 1952. It relates to the **annual registration required of osteopathic licentiates.** At the time of such annual registration, the applicant must show that he has attended during the prior year a one-day educational course or program of at least eight-hour duration approved by the board on subjects related to the practice of osteopathy and authorizes the board to accept as fulfilling such requirements attendance during at least one day of the two-day educational program conducted by the Michigan Osteopathy Association. H. 399, has become Public Act No. 83 of the Acts of 1952. It makes it a duty of the superintendent of public instruction to promote in the public schools of the state in normal colleges and universities in the state and among adult groups scientific instructions as to the **physical, psychological and sociological effects of alcohol** and the benefits of temperance.

The summary of federal legislation was prepared by the Washington Office of the American Medical Association and the summary of state legislation by the Bureau of Legal Medicine and Legislation.

Mississippi

Bill Introduced.—S. 304, proposes the creation in the office of the Attorney General of the **Mississippi Bureau of Investigation** which shall be provided with laboratory facilities for the analysis of evidence of crime, including the determination of presence, quantity and character of poisons, the character of blood stains, microscopic and other examination material associated with the commitment of crime, examination and analysis of projectiles of ballistic imprints and records which might lead to the determination or identification of criminals, the examination for and of finger prints, and other evidence leading to the identification, apprehension and conviction of criminals. S. 569, relating to **grants in aid for the construction of hospitals** and related institutions specifically included non-share corporations or foundations organized for medical and surgical purposes or for establishing, maintaining or operating clinical, pathological, medical or surgical research laboratories or hospitals, whose charter prohibit the reversion of any property of the corporation or foundation to any members, trustee, officer or other individual. S. 642, proposes an appropriation to the Board of Trustees of state institutions of higher learning for the purpose of paying for **scholarships for advanced studies in nursing.** S. 646, to amend the law relating to **privilege taxes upon businesses operating stores wherein eyes are examined,** proposes that nothing in the proposal shall be so construed as to prevent any person, firm or corporation from owning or operating a store or business establishment wherein eyes are examined or glasses fitted, provided that only a duly licensed optometrist shall examine the eyes of any person for the purpose of fitting the glasses.

New York

Bills Enacted.—A. 2636, has become Ch. 632 of the Laws of 1952. It amends the public health law by requiring physicians to report to the state department of health promptly the name and if possible the address of any person under treatment if it appears that such person is an **habitual user of any narcotic drug.** S. 2396, has become Ch. 530 of the Laws of 1952. It amends the education law by providing that no person shall falsely personate a licensed optometrist of a like or different name nor buy, sell or fraudulently obtain a license to practice optometry and it provides further that the **full name of the practitioner of optometry** must be displayed at the place where he practices. S. 2445, has become Ch. 557 of the Laws of 1952. It amends the education law by extending to July 1, 1953, certain licensing requirements applicable to **residents and interns** of state institutions. S. 2594, has become Ch. 624 of the Laws of 1952. It amends the public health law relating to **poliomyelitis** by authorizing local boards of health, after approval by the state commissioner of health, to provide at the remedial stages of the disease suitable surgical medical or therapeutic or hospital care.

Rhode Island

Bill Introduced.—S. 286, resolved that the general assembly requests the Governor to take action by executive order or otherwise to require the **state director of health,** and those chief medical assistants who are now alleged to be dividing their time between private practice of medicine and their state jobs and duties, to devote their entire time to the responsibilities of their official positions in the state department of health.

Virginia

Bills Enacted.—H. 225, has become Ch. 651 of the Laws of 1952. It provides regulations for the granting of **annual nursing scholarships.** H. 426, has become Ch. 525 of the Laws of 1952. It makes it unlawful for any employer to require any employee or applicant for employment to pay the **cost of a medical examination** or the cost of furnishing any records required by the employer as a condition of employment. H. 722, has become Ch. 698 of the Laws of 1952. It amends the **medical practice act** relating to persons applying to take the examination for medical licensure by providing that if the applicant shows that the medical school from which he graduated is approved by the Council on Medical Education and Hospitals and that other members of his graduating class from such medical school have been allowed to take the examination for medical licensure while the applicant was serving in the armed forces and if he further agrees that if he passes the examination he will begin and continue for at least five years thereafter **the practice of medicine in some rural county in the state,** then he shall be entitled to take the examination. The law further provides that if at any time he discontinues such practice within the five year period the licensure shall thereupon be revoked. S. 278, has become Ch. 690 of the Laws of 1952. It amends the medical practice act by authorizing persons who are **interning or taking residency training** in the state to extend the three-year period of training for two additional years before being required to obtain a license to practice medicine. S. 385, has become Ch. 641 of the Laws of 1952. It provides regulations for the granting of twenty annual **medical scholarships** to be awarded to Virginia students attending the Meharry Medical College at Nashville, Tennessee.

TELECAST, MAY 4, FROM ATOMIC MEDICAL LABORATORY

Experiments with new radioactive isotopes of potential significance to the further advancement of medicine will be shown Sunday, May 4, during a nationwide telecast from Brookhaven National Laboratories, an atomic energy station at Upton, Long Island, N. Y.

This will be the first time that mobile television cameras have been allowed in an atomic energy installation. The telecast, scheduled for 1:30-2:00 p. m. (E.D.S.T.) and sponsored by the American Medical Association in cooperation with the National Broadcasting Company, will originate from the hospital and medical division of the laboratory. The viewing public will be permitted to see the interior of the laboratory where radioactive isotopes are separated and processed and will witness some of the experiments in progress.

Scientific authorities will appear on the program to demonstrate the use of atomic medicine in practical application to patients and to conduct scientific experiments in medical and basic research. They include Dr. Lee E. Farr, chairman of the medical department at Brookhaven; Dr. Donald D. Van Slyke, research director of Eli Lilly Foundation and guest scientist at Brookhaven; Dr. F. Marott Sinex, a member of the staff at Brookhaven, and L. G. Stang, leader of the laboratory section where radioactive isotopes are separated and processed. The program will be narrated by Dr. W. W. Bauer, Chicago, Director of the Bureau of Health Education of the A. M. A., and Ben Grauer, New York, well-known announcer.

The medical department of Brookhaven has under its jurisdiction a 36-bed research hospital, the first to be developed solely for the study of atomic energy medicine. Patients, who come from all parts of the United States for study and treatment, are admitted only after referral by their physicians.

CIVIL DEFENSE DUTIES ASSIGNED TO DOCTORS

The King County Medical Society announced March 19 that it has completed the task of assigning each of its active member physicians (about 850) to specific Civil Defense duties in the event of any major emergency. The job has taken several months.

Cooperating with the City's Civil Defense Authorities the Medical Society early in 1951 took the responsibility of making certain that all first-aid stations, provisional hospitals, and regular hospitals in Seattle's civil defense planning would be properly manned by physicians during an atomic or other kind of city-wide disaster. During the next two weeks each physician actively practicing medicine and living within the confines of the city was notified just what his task would be and where he was to go during a civil defense emergency.

Zoning of the rest of King County, outside Seattle, and the designation of first-aid stations was completed by the Civil Defense Authorities by the middle of April, and assignments for King County physicians living beyond Seattle's city limits was made at that time.

The King County Medical Society also announced the formation of a standing Civil Defense Committee, with Dr. Bruce Zimmerman as chairman. The creation of such a committee is assurance to the citizens of Seattle that this city's Medical Civil Defense will be kept alive and up-to-date. Other members of the committee are Drs. Wallace D. Hunt, Raymond Zech, Vernon O. Lundmark, Simeon Cantril, John Lecocq, William Y. Baker, and Wayne Sims. Dr. John Culp will represent the King County Medical Society Board of Trustees on the committee.

Certain schools where first-aid stations are being set up were designated and certain other schools were designated to be used as provisional hospitals.

COMMISSION ON CHRONIC ILLNESS

The national Commission on Chronic Illness, under the direction of Dr. Dean W. Roberts, will survey 13,000 persons in 4,000 families in Baltimore, Md., in a study of chronic disease and the needs of the chronically ill. Dr. Roberts will assume his new duties as staff director of the commission on July 1, and the commission's office headquarters will be moved from Chicago to Baltimore at that time.

Dr. Roberts is on the faculty of Johns Hopkins University as a lecturer in public health administration and also gives annual lectures at Harvard, Yale, and the University of Maryland. Last summer, as consultant to the World Health Organization, Dr. Roberts conducted a survey of health conditions in northeast Brazil.

The Baltimore study of chronic disease among city dwellers is a companion to a previously announced study among the rural population in Hunterdon County, New Jersey. Results of medical studies of persons in the test groups found to be chronically ill will be evaluated to estimate their needs for medical care and related services. The studies are expected to reveal significant information on the extent of chronic disease present in both the urban and the rural population.

Dr. Roberts and the commission staff will begin in Baltimore a series of studies, planned to cover several years, of medical services and facilities needed by the chronically ill.

The commission was founded in 1949 by the American Hospital Association, American Medical Association, American Public Health Association, and the American Public Welfare Association.

The AMA has pledged continued financial support to the Commission on Chronic Illness in the amount of $80,000, to be paid over a four year period. This year's installment of $20,000 was recently turned over to the commission. A $300,000 budget set by the commission for the coming four year period has been met by 12 contributing organizations.

COMMITTEE ON MENTAL HEALTH

The first meeting of the Committee on Mental Health of the Board of Trustees (previously designated the Committee on Nervous and Mental Diseases), composed of Drs. Walter H. Baer, Leo Bartemeier, Hugh T. Carmichael, Francis M. Forster, M. Ralph Kaufman, Maurice Levine, and Lauren H. Smith, met at the headquarters of the American Medical Association on March 27, all members of the Committee being present. The following officers were elected: Dr. Leo Bartemeier, Chairman, and Dr. Lauren H. Smith, Vice Chairman. The Chairman, Vice Chairman, and Dr. Walter H. Baer were selected to serve as the executive committee of the Committee on Mental Health.

Many problems in the fields of psychiatry and neurology with which the Committee may concern itself were discussed. Plans were formulated for other meetings in the near future, and a report on actions that may be taken at these sessions will appear in subsequent issues of THE JOURNAL.

COUNCIL ON FOODS AND NUTRITION

Dr. James S. McLester, former President of the American Medical Association and professor emeritus of medicine at the University of Alabama, has retired as chairman of the American Medical Association's Council on Foods and Nutrition after 15 years of meritorious service. Dr. Philip C. Jeans, professor of pediatrics at the University of Iowa School of Medicine, is his elected successor. A portrait of Dr. McLester, presented to the Board of Trustees of the American Medical Association by the Council in Dr. McLester's honor, will be hung at the Association headquarters in Chicago.

MEDICAL NEWS

CALIFORNIA

Personals.—Dr. Hall G. Holder has resigned as chief of surgery at the San Diego County Hospital. He had been on the surgical staff since 1927.——Dr. Richard W. Lippman, research associate, Institute for Medical Research, Cedars of Lebanon Hospital, Los Angeles, has been elected chairman of the Southern California Section of the Society for Experimental Biology and Medicine for the academic year 1952-53.

Congenital Heart Disease.—The state department of public health has been allotted $36,201 by the United States Children's Bureau to administer a regional program for the benefit of children with congenital heart disease. California will now be able to receive children from Arizona, Idaho, Nevada, Alaska, and Hawaii who are referred to the department by various children's agencies. The handicapped children will, in turn, be referred for diagnosis and treatment to four hospitals and to practicing specialists. Hospitals participating in this program are Mount Zion, Stanford University and University of California in San Francisco, and the Children's Hospital in Los Angeles.

DISTRICT OF COLUMBIA

Dr. Claude Beck's Lecture.—Dr. Claude S. Beck, professor of neurosurgery, Western Reserve University School of Medicine, Cleveland, will deliver the annual Phi Delta Epsilon Lecture, sponsored by Psi Chapter, at the George Washington University School of Medicine. Dr. Beck will address the student body and members of the faculty in hall A of the medical school building at 12 noon, May 3 on "Operation for Coronary Artery Disease."

FLORIDA

Postgraduate Seminar.—Mount Sinai Hospital, Miami Beach, will hold its annual seminar May 22-24. "Recent Advances in Diagnosis and Treatment" will be discussed by Drs. James H. Means and William Dameshek, Boston; Drs. Delbert M. Bergenstal, Joseph B. Kirsner, and Rachmiel Levine, Chicago; Dr. Daniel C. Darrow, New Haven; Dr. J. William Hinton, New York, and Dr. Robert Elman, St. Louis. The registration fee of $20 will be omitted for interns and residents. The banquet fee will be $7.50.

ILLINOIS

Personal.—Dr. William M. Hanrahan, former director of the Brevard-Osceola Bi-County Health Department in Florida, has been appointed director of the Champaign-Urbana Public Health District.

Illinois Society for Medical Research.—To strengthen its program of public education concerning the use of animals in medical research and teaching, the Illinois Society for Medical Research is undertaking a campaign to increase its membership and financial support. Dr. Anton J. Carlson, Chicago, president of the society, states that solicitation of members will be based on three groups: individuals; associations and organizations, and institutions and businesses. The total sum expected to be raised for the current year is $10,000.

Chicago

Society News.—The Chicago Gynecological Society held a joint meeting with the St. Louis Gynecological Society and the Kansas City Obstetrical and Gynecological Society April 18. Out-of-state speakers were Drs. George J. L. Wulff and Alva C. Trueblood of St. Louis, who spoke on "Breech Delivery," and Dr. Kenneth E. Cox, Kansas City, Mo., who discussed "The Role of Colpoclysis in Vaginal Fistulae."

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

Lectures on Medical History.—The medical school of Northwestern University is conducting a series of free lectures on the history of medicine from 5 to 6 on Tuesday evenings at Thorne Hall on the Chicago campus. Remaining lectures are as follows:

April 30, Loyal Davis, chairman of the department of surgery, Stormy Petrel of Surgery (John B. Murphy).
May 7, Vincent J. O'Conor, chairman of the department of urology, Development of Urinary Antiseptics.
May 14, Abraham Levinson, professor of pediatrics, History of Pediatrics.
May 21, William J. Ford, instructor in medicine, John Hunter, the Great English Anatomist of the Late 18th Century.
May 28, William B. Wartman, professor of pathology, History of Tumors.
June 4, Herbert Rattner, professor of dermatology, Ordinary Baldness.

Chicago Medical School Grants.—At a recent fund raising dinner given by Dr. Sydney R. Bazell, assistant in the department of dermatology and syphilology, $22,000 was contributed for the benefit of the Chicago Medical School. On May 3 the Faculty Wives Association is sponsoring a concert at Orchestra Hall for the benefit of the school, at which Marian Anderson will be the soloist.

Recent research grants and renewals of former grants for studies of hypertension and cancer total $53,976. Dr. Hans Elias, assistant professor of the department of anatomy, receives $4,320 from the National Heart Institute for "study of the three dimensional structure of the human adrenal cortex in normal and hypertensive persons." Dr. Israel Davidsohn, professor and chairman of the department of pathology and pathologist and director of laboratories at Mount Sinai Hospital, received a renewal of $13,068 from the U. S. Public Health Service for continuation of studies of "natural and immune antibodies in inbred mouse strains with low and high tumor incidence." He has also received a grant of $6,598 for research in hemolytic anemia. Dr. Philippe Shubik, coordinator of oncology, has received a renewal of $25,000 from the National Cancer Institute to be used for cancer teaching and $5,000 as a second payment of a grant from the same source for "study of successive stages of carcinogenesis."

MASSACHUSETTS

Myerson Memorial Laboratory.—This laboratory at Boston State Hospital was dedicated Jan. 3 to the memory of the late Dr. Abraham Myerson, who for 36 years served on the medical staff and was director of research for 26 years. Dr. Israel S. Wechsler, clinical professor of neurology at Columbia University, New York, reviewed Dr. Myerson's career as a clinician, teacher, and scientist; other papers were presented by the hospital staff. Dr. Jack R. Ewalt, commissioner of the state department of mental health, gave the closing address on "The Importance of Research in Psychiatry."

Evening Lectures.—The House Officers' Association of the Boston City Hospital announces the following programs to complete its evening lecture series for 1951-1952:

May 6, Introduction to Vector Electrocardiography, Robert P. Grant, Baltimore.
May 9, Nature of the Electrocardiographic Changes in Coronary Occlusion (illustrated by high speed motion picture film), Myron Prinzmetal, San Francisco.
May 15, Treatment of Epilepsy (with illustration by the film "Seizure"), William G. Lennox, Boston.
May 20, Respiratory and Metabolic Aspects of Acid-Base Control During Anesthesia, Emanuel M. Papper, New York.
May 27, Pathogenesis of Essential Hypertension, Ephraim Shorr, New York.
May 29, Pulmonary Air Cysts: Some Diagnostic, Functional and Therapeutic Considerations, K. Albert Harden, Washington, D. C.
June 3, Pulmonary Function Tests, Julius H. Comroe, Philadelphia.

These programs are held at 7 p. m. in the new Cheever Amphitheatre of the Dowling Building of Boston City Hospital.

NEBRASKA

State Medical Meeting in Lincoln.—The Nebraska State Medical Association will hold its annual session May 12-15 at the Hotel Cornhusker in Lincoln under the presidency of Dr. Donald B. Steenburg, Aurora. The program includes panel discussions on "Emergencies of the Newborn," "Cancer," and "Some Clinical Aspects of Abnormal Calcium and Phosphorus Metabolism," and a symposium on immunology and hematology. Out-of-state speakers include:

James M. Baty, Boston, Pyuria in Children.
Carroll Z. Berman, Boston, Radiological Aspect of the Diagnosis of Chronic Abdominal Pain in Children.
Orvar Swenson, Boston, Megacolon.
Jerome W. Conn, Ann Arbor, Present Status of ACTH and Cortisone in Clinical Practice.
Arthur C. Curtis, Ann Arbor, Contact and Occupational Dermatoses.
Reed M. Nesbit, Ann Arbor, Problems Relating to the Recognition of Hydronephrosis in Every Day Practice.
Donald A. Dukelow, Chicago, The School Health Problem in Nebraska.
Robert S. Sparkman, Dallas, Common Fallacies Concerning Gallbladder Disease.
Sol Haberman, Ph.D., Dallas, Rational Use of Antibiotics.
Joseph M. Hill, Dallas, Diagnosis and Treatment of Anemias.

At the banquet May 14 Raymond Moley, Ph.D., New York, editor of *Newsweek*, will speak on "How to Keep Our Liberty." The woman's auxiliary will meet at the same time.

NEW JERSEY

Personals.—Dr. Hyman I. Goldstein, Camden, has been voted to life membership in the Philadelphia Pediatric Society, in which he has been active for nearly 40 years. Dr. Goldstein was recently appointed a delegate to the third European Congress of National Societies of Gastroenterology held in Bologna, Italy, April 20-26, and also to the third Pan-American Working Day of Gastroenterology to be held in Mexico City, May 11-17.

State Medical Meeting in Atlantic City.—The annual meeting of the Medical Society of New Jersey will be held at Haddon Hall, Atlantic City, May 19-21 under the presidency of Dr. Sigurd W. Johnsen, Passaic. There will be 12 section meetings. The section on surgery will present a panel discussion on cancer of the breast at 2 p. m. May 21. Participants, all of Columbia University College of Physicians and Surgeons, New York, will be Drs. Cushman D. Haagensen, associate professor of clinical surgery, Maurice Lenz, professor of clinical radiology, and Arthur Purdy Stout, professor of pathology. Section luncheon meetings will be held daily. A banquet will follow the president's reception, which will be held May 20, 6:30 p. m. The woman's auxiliary will have its annual meeting simultaneously.

NEW YORK

Lecture on Isotopes.—The Council Committee on Public Health and Education of the Medical Society of the State of New York, in cooperation with the New York State Department of Health, announces a lecture to be given for the Queens County Medical Society on May 2 at 4 p. m. at Queens County Medical Society Building, 112-25 Queens Blvd., Forest Hills. Dr. Edith H. Quimby, Sc.D., associate professor of radiology, Columbia University College of Physicians and Surgeons, will speak on "Diagnostic Procedures with Radioactive Isotopes."

Annual State Medical Meeting.—The annual convention of the Medical Society of the State of New York will be held May 12-16 at the Hotel Statler in New York. Television Teaching Day will be devoted to television in color showing techniques of diagnostic and therapeutic procedures. These presentations will be made in cooperation with New York University College of Medicine, New York University Post-Graduate Medical School, and Bellevue Hospital, at which the demonstrations will originate. The morning program will be on biopsy of sternal bone marrow, biopsy of liver, gastroscopy, venous pressure and circulation times, maximum breathing capacity, division of lung air and other tests of respiratory function, lumbar sympathetic block, and technics of administering fluids and blood to infants. The afternoon program will be devoted to a demonstration of auscultation of the heart, making use of the latest electronic instruments, and a clinicopathological conference. The color telecasts will continue through the convention. There will be scientific section meetings, and sessions on the history of medicine and public relations. At a symposium on neonatal mortality May 14 at 2:30 p. m. the following papers will be presented:

Edward R. Schlesinger, Albany, Fetal and Neonatal Mortality.
Alfred J. Vignec, New York, Recent Trends in Premature Care.
Sidney Farber, Boston, Some Aspects of Neonatal Pathology.
Louis M. Hellman, Brooklyn, Newer Concepts in the Use of Analgesics and Anesthetics for Labor and Delivery.

A banquet will be held in the Penn Top on May 14 at 7 p. m. The woman's auxiliary will meet at the Statler May 11-15.

New York City

The Freud Lecture.—Under the sponsorship of the New York Psychoanalytic Society and Institute, the Freud lecture, "Psychoanalysis and the Study of Creative Imagination," will be given by W. Ernst Kris, Ph.D., May 6 at 8:30 p. m. in Hosack Hall, The New York Academy of Medicine, 2 E. 103rd St.

Gift for Student Residence at Cornell.—The Olin Foundation has given $2,549,000 to provide a student residence for Cornell University Medical College. Preliminary plans call for a 12-story building with 250 rooms for students and 25 for visiting scientists, alumni, and parents. The building will also include offices, meeting rooms, lounges, snack bar, and athletic facilities.

Psychiatrists Wanted.—The Municipal Civil Service Commission of the City of New York is reopening the application period for psychiatrist, grade 4. Applications will be issued April 15-30. Persons who filed in January need not file application again but may make amendments or additions thereto. There are 26 vacancies in the department of hospitals at yearly salaries of $6,650, including an annual cost of living adjustment of $250. Information may be obtained from the office at 299 Broadway, New York 7.

PENNSYLVANIA

General Practice Meeting.—The Pennsylvania Academy of General Practice will hold its convention in Bedford Springs May 9-11. The program being presented on Saturday includes the following visiting speakers:

Frank N. Wilson, Ann Arbor, Subject to be announced.
Philip Thorek, Chicago, The Acute Abdomen.
Walter J. Reich, Chicago, Office Gynecology.

The program will close with a panel discussion on cerebral vascular accidents.

Meeting on Tumors.—The Wainwright Tumor Clinic Association of Pennsylvania under the direction of the commission on cancer of the Medical Society of the State of Pennsylvania will hold its annual meeting in the Masonic Building in Allentown May 14. Visiting speakers and their subjects include:

William A. Cooper, New York, The Gastric Cancer Problem.
Harry M. Weber, Rochester, Minn., Roentgenologic Diagnosis of Cancer of the Upper Gastrointestinal Tract.
Charles S. Cameron Jr., New York, Observations and Suggestions in the Early Diagnosis of Cancer.

The luncheon speaker will be Dr. Harold L. Foss, president-elect of the American College of Surgeons, who will speak on "What the American College of Surgeons Is Doing About Cancer."

Annual Academy Meeting.—The Pennsylvania Academy of Ophthalmology and Otolaryngology will hold its annual meeting May 8-11 at Galen Hall Hotel, Wernersville (Reading). Guest speakers will include Drs. M. Royden C. Astley and Edmund B. Spaeth, Philadelphia; Ben H. Senturia and James B. Costen, St. Louis; Olav E. Hallberg, Rochester; Herman Elwyn, New York; Lawrence R. Boies, Minneapolis; Alson E. Braley and Dean M. Lierle, Iowa City; William C. Owens, Baltimore, and Paul A. Chandler, Boston. The program will also include conferences and courses, study club presentations, motion pictures, and a golf tournament. The academy has inaugurated a state program for testing and disposition of 50,000 deafened school children.

Philadelphia

Hospital Affiliates with University.—The Skin and Cancer Hospital in Philadelphia has announced that it will become affiliated formally with the Graduate School of Medicine of the University of Pennsylvania following a program of special service during the past 26 years.

Personal.—Dr. Chevalier L. Jackson, president of the American College of Chest Physicians, was honored by the Cuban chapter of the college during a recent visit to Cuba. Dr. Jackson, guest of honor of the III Pan-American Congress of the International Society for Otorhinolaryngology, received a certificate from the Pan-American Colombist Society for his many years of devoted service to the Latin American countries in the field of medicine.

Appoint Director of Phipps Institute.—Dr. Julius L. Wilson, formerly head of the chest division of the Ochsner Foundation Clinic, New Orleans, has been named director of the Henry Phipps Institute and professor of medicine at the University of Pennsylvania. Dr. Wilson has served as chairman of the health division and a member of the board of directors of the New Orleans Council of Social Agencies. He has been a member of the board of the Louisiana Tuberculosis Association since 1939 and program director of the New Orleans Tuberculosis Association since 1938.

TEXAS

Dr. Leake to Study Papyri.—Chauncey D. Leake, Ph.D., of the University of Texas Medical Branch, Galveston, has been given a leave of absence for special work on old Egyptian medical papyri at the Institute for Advanced Study, Princeton, N. J. He will give a series of talks at eastern institutions on this subject during April. On April 15 he spoke at the Army Medical Library, Washington, D. C., on "Leonardo da Vinci: Scientist and Artist," commemorating the 500th anniversary of the birth of da Vinci.

Grants for Research.—The Caruth Foundation of Dallas has made two grants to the Southwestern Medical School of the University of Texas, Dallas, through the Southwestern Medical Foundation. A grant of $4,000 will be used for research in the department of pediatrics under the direction of Dr. James J. Quilligan, associate professor. Influenza and other related virus diseases will be studied by Dr. Quilligan and his associates. A $5,000 grant for research in the department of bacteriology, under the direction of S. Edward Sulkin, Ph.D., professor and chairman of the department of bacteriology, will be utilized for the study of mechanisms involved in the control of virus diseases in humans.

WEST VIRGINIA

Appoint Health Education Consultant.—Fred J. Holter, Ph.D., of Morgantown has been named health education consultant to the state department of health. He has been a college teacher, specializing in health education since 1929 and joined the staff at West Virginia University in 1947. The appointment of Dr. Holter follows closely the recommendation of those attending the fourth annual rural health conference at Jackson's Mill last September that a consultation service on community health be established within the state. The conference was sponsored by the West Virginia State Medical Association. Dr. Holter will be available for consultant services in communities interested in organizing community health councils. Only eight communities in West Virginia now have active councils, and health officials feel that several additional councils are needed in various parts of the state.

HAWAII

Territorial Medical Meeting.—The Hawaii Territorial Medical Association will hold its annual meeting in the Mabel Smyth Building, Honolulu, May 1-4 under the presidency of Dr. Harry L. Arnold Jr., Honolulu. Visiting speakers will be Dr. William Boyd, Toronto, who will speak on "Pathology of the Ground Substance of the Mesenchyme," and Dr. Howard W. Bosworth, Los Angeles, who will speak on "Evaluation of Methods of Treatment of Pulmonary Tuberculosis."

GENERAL

Bequest for Health Program in Israel.—A gift of $170,000 from the estate of the late Florina Lasker, New York civic and social worker, has been made to Hadassah on its 40th anniversary. The money will be used to further Hadassah's health and welfare program in Israel. Miss Lasker died in September, 1949.

Dr. Bortz to Address Drug Manufacturers.—Dr. Edward L. Bortz, Philadelphia, former president of the American Medical Association, will speak at the annual meeting of the American Drug Manufacturers Association at the Homestead, Hot Springs, Va., April 28 to May 1. His address, "The Challenge of the Increasing Life Span of Our Population," will be delivered at the general session April 30.

Vaccinations for Travelers.—A list of vaccinations required of travelers in 183 countries and territories is available at the Pan-American Sanitary Building, the regional office of the World Health Organization, 1501 New Hampshire Ave., N. W., Washington, D. C. The vaccinations most generally required are against smallpox, yellow fever, and cholera. Several countries also insist on vaccination against typhoid and paratyphoid fevers, typhus, diphtheria, and tetanus.

Volume in Honor of Colonel Craig.—Pursuant to the merging of the American Society of Tropical Medicine and the National Malaria Society, the respective journals of these societies, the *American Journal of Tropical Medicine* and the *Journal of the National Malaria Society*, have been fused into one official organ, the *American Journal of Tropical Medicine and Hygiene*. The first issue of this publication, the January number, is a commemorative volume in honor of the late Dr. Charles Franklin Craig, colonel, U. S. Army Medical Corps, retired.

Annual Award for Clinical Chemistry.—The Ernst Bischoff Award of the American Association of Clinical Chemists, Inc., will be presented annually to a chemist on the staff of a hospital or clinical chemistry laboratory who has distinguished himself by achievement and devotion and has helped to solve those chemical problems that arise daily in the practice of the medical arts. The recipient of the award will receive $500, a scroll, and specially designed bronze medal. John G. Reinhold, Ph.D., Philadelphia, president of the association, has appointed Harry H. Sobotka, Ph.D., Mount Sinai Hospital, New York, chairman of the first award committee.

Dr. Wegman to Head Division of Education.—Dr. Myron E. Wegman, head of the department of pediatrics at the Louisiana State University School of Medicine, New Orleans, has been appointed to the staff of the Pan American Sanitary Bureau, regional office of the World Health Organization, to take charge of its newly-created division of education, training and technical services. He will assume duties June 1. Dr. Wegman is a member of the WHO Expert Committee on School Health Services and, as a consultant for the organization, has made comprehensive field surveys in Europe and South America.

Meeting of College Health Association.—The American College Health Association will hold its annual meeting May 1-3 at the Copley Plaza Hotel in Boston under the presidency of Dr. John E. Sawhill, New York. The program will include presentations on "Antibiotics in the Management of Common Infectious Diseases" by Dr. Chester S. Keefer, Wade Professor of Medicine, Boston University School of Medicine; "The Serious Recurrent Injuries of Athletics—Contraindications for Further Competitive Participation" by Dr. Augustus Thorndike, chief surgeon, department of hygiene, Harvard Medical School and Harvard Athletic Association, and "Impressions of Student Health Services in Great Britain" by Dr. Ruth E. Boynton, director of the students' health service at the University of Minnesota.

Conference on Administrative Medicine.—Authorities on administrative medicine from New York, Philadelphia, Pittsburgh, and Detroit will meet in the McMillin Academic Theater on the Columbia University campus May 15 at 9:30 a. m. to discuss "Current Problems in Administrative Medicine." The conference, sponsored by the Institute of Administrative Medicine of the Columbia School of Public Health, is designed not only for the

medical profession but also for industrial and business executives, personnel directors, and other interested nonmedical persons. Guest sepakers will include Dr. Ephraim M. Bluestone, consultant at Montefiore Hospital, New York; Dr. James P. Dixon, commissioner of health, Philadelphia; Mr. Winslow Carlton, chairman of the board, Group Health Insurance, Inc., New York; and Dr. Leslie A. Falk, area medical administrator, United Mine Workers of America, Welfare and Retirement Fund, Pittsburgh.

National Hearing Week.—The educational campaign of National Hearing Week, May 4-10, aims to acquaint the public with existing programs for prevention of deafness, conservation of hearing, and rehabilitation of the hard of hearing. Dr. Thomas L. Tolan, Milwaukee, head of the American Hearing Society, stresses the fact that, in addition to the 115 chapters now affiliated with the society, there is urgent need for more chapters and extended services for the estimated 15 million acoustically handicapped children and adults in this nation. The American Hearing Society, a nonprofit, social service agency, promotes hearing conservation in schools; stimulates research; guides member hearing societies in 34 states, the District of Columbia, and Canada; publishes *Hearing News,* a monthly magazine; distributes hearing literature; provides field service throughout America in connection with community hearing programs, and furnishes information for individuals and organizations all over the world.

Surgeons Meeting in Colorado Springs.—A meeting of the Rocky Mountain District of the United States and Canadian chapters of the International College of Surgeons will be held at the Broadmoor Hotel, Colorado Springs, Colo., May 2-3. Participating provinces and states are Alberta, Montana, Idaho, Wyoming, Utah, Colorado, Arizona, and New Mexico. Among the papers to be presented are the following:

William Carpenter MacCarty, Rochester, Minn., UNESCO and its Efforts to Organize Medical and Scientific Congresses.
William R. Oakes, Los Alamos, N. M., Course of Testicular Injury Following Accidental Exposure to Nuclear Radiation: Report of a Case.
Archibald R. Buchanan, Denver, Fascial Planes of the Neck.
E. Stewart Taylor, Denver, Diagnostic Difficulties Surrounding Surgical Treatment of Hydatid Mole and Choriocarcinoma.
Thomas F. Keyes, Salt Lake City, Surgery of the Heart and Great Vessels.
James E. Musgrove, Albuquerque, N. M., Emergency Surgery of the Newborn.
Glenn W. Koford, Cheyenne, Wyo., Kielland Forceps in Persistent Occiput Posterior Presentation.
James M. Ovens, Phoenix, Ariz., Command Operation and Its Modifications.
Clarence N. Sorensen, Scottsbluff, Neb., Plain Film Study of the Abdomen.
Vernon L. Bolton, Colorado Springs, Colo., Radiology of Prolapsed Gastric Mucosa.
Erving F. Geever, Colorado Springs, Colo., Direct Tissue Studies with the Electron Microscope.
William A. Campbell Jr., Colorado Springs, Colo., Cardiac Arrest.

LATIN AMERICA

Society Election.—Officers elected at the annual session of the Sociedad Mexicana de Oftalmologia on Feb. 12 include Dr. Daniel Silva, president; Dr. Manuel de Rivas Cherif, vice-president; Dr. Raul A. Chavira, permanent secretary, and Dr. Roberto Quiroz B., annual secretary.

University Appointment.—Dr. Waldemar Bianchi, who went to the Mayo Foundation in Minnesota as a graduate student in physical medicine under the auspices of the Institute of Inter-American Affairs in 1946, has been appointed professor of physical medicine of the Faculdade de Ciencias Medicas, University of the Federal District, Rio de Janeiro.

CORRECTION

Therapeutic Experiments in Female Infertility.—In the article on this subject in THE JOURNAL, Feb. 23, 1952, page 604, reference was made to the British branch of the Schering Corporation. The firm referred to was British Schering Limited, which has no connection whatsoever with the Schering Corporation in the United States.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 24-26, 1952. Sec., Dr. D. G. Gill, 537 Dexter Ave., Montgomery 4.

ALASKA:* *Examination.* Juneau. On application in other towns where there are board members. *Reciprocity.* On application. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARKANSAS:* *Examination. Regular.* Little Rock, June 5-6. Sec., Dr. Joe Verser, Harrisburg. *Homeopathic.* Little Rock, June 10-11. Sec., Dr. Carl S. Bungart, 105 N. 14th St., Fort Smith. *Eclectic.* Little Rock, June 5-6. Sec., Dr. Frank C. Smith, 2301 Broadway, Little Rock.

CALIFORNIA: *Written.* San Francisco, June 23-26; Los Angeles, Aug. 18-21; Sacramento, Oct. 20-23. Application must be received at least two weeks prior to date of examination. *Oral for Reciprocity Applicants.* San Francisco, June 21; Los Angeles, Aug. 16; San Francisco, Nov. 8. Applicants are requested not to arrange to come to an oral examination until they receive notice from the Credentials Committee. *Oral and Clinical for Foreign Medical School Graduates.* San Francisco, June 22; Los Angeles, Aug. 17; San Francisco, Nov. 9. Sec., Dr. Frederick N. Scatena, 1020 N St., Sacramento.

COLORADO:* *Examination.* Denver, June 10-12. Final date for filing application is May 12. *Reciprocity.* Denver, April 8. Final date for filing application was Mar. 10. Sec., Dr. Samuel H. Brown, 831 Republic Bldg., Denver.

DELAWARE: Dover, July 8-10. Sec., Dr. Joseph S. McDaniel, 229 South State St., Dover.

FLORIDA:* *Examination.* Jacksonville, June 29-July 1. Sec., Dr. Homer L. Pearson, 701 Dupont Bldg., Miami.

GEORGIA: Atlanta and Augusta, June. Sec., Mr. R. C. Coleman, 111 State Capital, Atlanta 3.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. Austin W. Matthis, Agana.

HAWAII: *Examination.* Honolulu, July 14-17. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

IDAHO: Boise, July 14-16. Sec., Mr. Armand L. Bird, 305 Sun Bldg., Boise.

ILLINOIS: *Examination.* Chicago, June 24-26 and Oct. 7-9. Supt. of Regis., Mr. Charles F. Kervin, Capitol Bldg., Springfield.

INDIANA: Indianapolis, June 1952. Sec., Dr. Paul R. Tindall, 1138 K of P Bldg., Indianapolis 4.

IOWA:* *Examination.* Iowa City, June 9-11. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Kansas City, June 4-5. Sec., Dr. O. W. Davidson, 864 New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, June 3-5. Sec., Dr. Bruce Underwood, 620 S. Third St., Louisville.

MARYLAND: *Examination.* Baltimore, June 17-20. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, June 17-18. Sec., Dr. John A. Evans, 6029 Bellona Ave., Baltimore.

MICHIGAN:* *Examination.* June. Sec., Dr. J. E. McIntyre, 100 W. Allegan St., Lansing 8.

MISSOURI: *Examination.* St. Louis, May 28-29 and June 13-14. *Reciprocity.* May 27. Ex. Sec., Mr. John A. Hailey, Box 4, State Capitol Bldg., Jefferson City.

NEBRASKA: *Examination.* Omaha, June 16-18. Director, Mr. Husted K. Watson, Bureau of Examining Boards, Room 1009, State Capitol, Lincoln.

NEW JERSEY: *Examination.* Trenton, June 17-20. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO:* Santa Fe, April 14-15. Sec., Dr. Charles J. McGoey, Coronado Bldg., Santa Fe.

NORTH CAROLINA: *Reciprocity.* Pinehurst, May 5. *Written.* Raleigh, June 16-19; *Reciprocity.* Raleigh, June 17. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, July 9-11. *Reciprocity.* Grand Forks, July 12. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Examination.* Columbus, June 17-20. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

OKLAHOMA:* *Examination.* Oklahoma City, June 4-5. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Reciprocity.* Portland, April 18-19. *Examination.* Portland, July. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

SOUTH CAROLINA: *Reciprocity.* Columbia, April 7. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA:* Rapid City, July 15. Sec., Dr. C. B. McVay, Yankton Clinic, Yankton.

TEXAS: Fort Worth, June 19-21. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth.

UTAH: *Examination.* Salt Lake City, July. Asst. Dir., Mr. Frank E. Lees, 314 State Capitol Bldg., Salt Lake City 1.

VIRGINIA: *Examination.* Richmond, June 12-14. *Reciprocity.* Richmond, June 11. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.

VIRGIN ISLANDS: St. Thomas, June 4-5. Sec., Dr. Earle M. Rice, St. Thomas.

WEST VIRGINIA: Charleston, April 7-8. Sec., Dr. H. H. Dyer, State Office Bldg. No. 3, Charleston 5.

WASHINGTON: Seattle, July. Sec., Mr. Edward C. Dohm, Department of Licenses, Olympia.

WISCONSIN:* Milwaukee, July 8-10. Sec., Dr. A. G. Koehler, 46 Washington Blvd., Oshkosh.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination.* On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

ARKANSAS: *Examination.* Little Rock, May 1-2. Sec., Mr. L. E. Gebauer, 1002 Donaghey Bldg., Little Rock.

DISTRICT OF COLUMBIA: *Examination.* Washington, April 21-22. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington, D. C.

FLORIDA: Gainesville, June 7. *Examination.* Sec., Mr. M. W. Emmel, Box 340, University of Florida, Gainesville.

MICHIGAN: *Examination.* May. Sec., Miss Eloise LeBeau, 501 W. Michigan Ave., Lansing 15.

OKLAHOMA: *Examination.* Oklahoma City, April 14. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, June 7, Sept. 6 and Dec. 6. Sec., Dr. Charles D. Byrne, State Board of Higher Education, University of Oregon, Eugene.

SOUTH DAKOTA: Vermillion, June 13-14. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

TEXAS: Austin, April 18-19. *Examination.* Examination may also be given in Galveston, Dallas and Houston. Sec., Bro. Raphael Wilson, 306 Nalle Bldg., Austin.

WISCONSIN: *Examination.* Milwaukee, June 7 and Sept. 13. Sec., Mr. W. H. Barber, Ripon College, Ripon.

* Basic Science Certificate required.

MEETINGS

American Medical Association, Chicago, June 9-13. Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

AMERICAN ACADEMY OF PEDIATRICS, Areal Meeting, Hotel Statler, Washington, D. C., May 22-24. Dr. E. H. Christopherson, 636 Church St., Evanston, Ill., Executive Secretary.

AMERICAN ACADEMY OF TUBERCULOSIS PHYSICIANS, Chicago, June 7. Dr. Oscar S. Levin, P. O. Box 7011, Denver, Secretary.

AMERICAN ASSOCIATION FOR THORACIC SURGERY, Dallas, Texas, May 8-10. Dr. Paul C. Samson, 2938 McClure St., Oakland 9, Calif., Secretary.

AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS, Seaview Country Club, Absecon, N. J., June 19-21. Dr. Norris J. Heckel, 122 South Michigan Ave., Chicago 3, Secretary.

AMERICAN ASSOCIATION OF THE HISTORY OF MEDICINE, Kansas City, Kans., May 1-3. Dr. Iago Galdston, 2 East 103d St., New York 29, Secretary.

AMERICAN ASSOCIATION ON MENTAL DEFICIENCY, Philadelphia, May 20-24. Dr. Neil A. Dayton, P. O. Box 96, Willimantic, Conn., Secretary.

AMERICAN BLOOD IRRADIATION SOCIETY, Conrad Hilton Hotel, Chicago, June 7-8. Dr. H. T. Lewis, 5230 Center Ave., Pittsburgh, Secretary.

AMERICAN BRONCHO-ESOPHAGOLOGICAL ASSOCIATION, Royal York Hotel, Toronto, Canada, May 20-21. Dr. Edwin N. Broyles, 1100 North Charles St., Baltimore 1, Secretary.

AMERICAN COLLEGE OF CHEST PHYSICIANS, Congress Hotel, Chicago, June 5-8. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago, Executive Secretary.

AMERICAN COLLEGE HEALTH ASSOCIATION, Copley Plaza Hotel, Boston, May 1-3. Miss Edith M. Lindsay, School of Public Health, University of California, Berkeley 4, Calif., Secretary.

AMERICAN COLLEGE OF SURGEONS, SECTIONAL MEETINGS:
Toronto, Canada, Royal York Hotel, May 15-17. Dr. Stuart D. Gordon, 170 St. George St., Toronto 5, Canada, Chairman.

AMERICAN DIABETES ASSOCIATION, Drake Hotel, Chicago, June 7-8. Dr. J. A. Reed, 11 West 42d St., New York 36, Secretary.

AMERICAN ELECTROENCEPHALOGRAPHIC SOCIETY, Hotel Claridge, Atlantic City, N. J., May 10-11. Dr. John A. Abbott, Massachusetts General Hospital, Boston 14, Secretary.

AMERICAN FEDERATION FOR CLINICAL RESEARCH, Haddon Hall, Atlantic City, N. J., May 4. Dr. Stewart Wolf, 525 East 68th St., New York 21, Secretary.

AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION, Hotel Claridge, Atlantic City, N. J., May 2-3. Dr. Dwight L. Wilbur, 655 Sutter St., San Francisco 2, Secretary.

AMERICAN GASTROSCOPIC SOCIETY, Hotel Claridge, Atlantic City, N. J., May 2-3. Dr. H. Marvin Pollard, University Hospital, Ann Arbor, Mich., Secretary.

AMERICAN GERIATRICS SOCIETY, Hotel LaSalle, Chicago, June 5-7. Dr. Malford W. Thewlis, 25 Mechanic St., Wakefield, R. I., Secretary.

AMERICAN GOITER ASSOCIATION, Chase Hotel, St. Louis, May 1-3. Dr. George C. Shivers, 100 East St. Vrain St., Colorado Springs, Colo., Secretary.

AMERICAN GYNECOLOGICAL SOCIETY, The Homestead, Hot Springs, Va., May 12-14. Dr. John I. Brewer, 104 South Michigan Ave., Chicago, Secretary.

AMERICAN LARYNGOLOGICAL ASSOCIATION, Royal York Hotel, Toronto, Canada, May 23-24. Dr. Louis H. Clerf, 1530 Locust St., Philadelphia 2, Secretary.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, Royal York Hotel, Toronto, Canada, May 20-22. Dr. C. Stewart Nash, 277 Alexander St., Rochester 7, N. Y., Secretary.

AMERICAN MEDICAL WOMEN'S ASSOCIATION, Chicago, June 8. Dr. Irma Henderson-Smathers, 610 Medical Bldg., Asheville, N. C., Corresponding Secretary.

AMERICAN NEUROLOGICAL ASSOCIATION, Hotel Claridge, Atlantic City, N. J., May 8-10. Dr. H. Houston Merritt, 710 West 168th St., New York 32, Secretary.

AMERICAN OPHTHALMOLOGICAL SOCIETY, Hot Springs, Va., June 5-7. Dr. Maynard C. Wheeler, 30 West 59th St., New York 19, Secretary.

AMERICAN OTOLOGICAL SOCIETY, Royal York Hotel, Toronto, Canada, May 18-19. Dr. John R. Lindsay, 950 East 59th St., Chicago 37, Secretary.

AMERICAN PEDIATRIC SOCIETY, Hotel Chamberlin, Old Point Comfort, Va., May 7-9. Dr. Alms C. McGuiness, 237 Medical Laboratories, Univ. of Pennsylvania, Philadelphia 4, Secretary.

AMERICAN PROCTOLOGIC SOCIETY, Milwaukee, June 4-7. Dr. Stuart T. Ross, 131 Fulton Ave., Hempstead, L. I., N. Y., Secretary.

AMERICAN PSYCHIATRIC ASSOCIATION, Atlantic City, N. J., May 12-16. Dr. R. Finley Gayle Jr., 6300 Three Chopt Rd., Richmond 21, Va., Secretary.

AMERICAN PSYCHOANALYTIC ASSOCIATION, Chalfonte-Haddon Hall, Atlantic City, N. J., May 8-11. Dr. LeRoy M. A. Maeder, 1910 Rittenhouse Square, Philadelphia 3, Secretary.

AMERICAN RADIUM SOCIETY, Chicago, June 8. Dr. John Wirth, 635 Herkimer St., Pasadena 1, Calif., Secretary.

AMERICAN RHEUMATISM ASSOCIATION, Conrad Hilton Hotel, Chicago, June 6-7. Dr. William H. Kammerer, 33 East 61st St., New York 21, Secretary.

AMERICAN SOCIETY FOR CLINICAL INVESTIGATION, Atlantic City, N. J., May 5. Dr. William M. M. Kirby, Univ. of Washington School of Medicine, Seattle 5, Secretary.

AMERICAN SOCIETY FOR THE STUDY OF STERILITY, Chicago, June 7-8. Dr. Walter W. Williams, 20 Magnolia Terrace, Springfield 8, Mass., Secretary.

AMERICAN THERAPEUTIC SOCIETY, Blackstone Hotel, Chicago, June 5-8. Dr. Oscar B. Hunter Jr., 915 Nineteenth St. N.W., Washington 6, D. C., Secretary.

AMERICAN TRUDEAU SOCIETY, Hotel Statler, Boston, May 26. Dr. John D. Steele, 1790 Broadway, New York 19, Secretary.

AMERICAN VENEREAL DISEASE ASSOCIATION, Washington, D. C., May 1-2. Dr. William L. Fleming, 750 Harrison Ave., Boston 18, Secretary.

ARIZONA MEDICAL ASSOCIATION, Hotel Westward Ho, Phoenix, April 30-May 3. Dr. Frank J. Milloy, 15 E. Monroe St., Phoenix, Secretary.

ASSOCIATION OF AMERICAN PHYSICIANS, Atlantic City, N. J., May 6-7. Dr. Henry M. Thomas Jr., 1201 North Calvert St., Baltimore 2, Secretary.

CALIFORNIA MEDICAL ASSOCIATION, Biltmore Hotel, Los Angeles, April 27-30. Dr. Albert C. Daniels, 450 Sutter St., San Francisco 8, Secretary.

CATHOLIC HOSPITAL ASSOCIATION OF THE UNITED STATES AND CANADA, Cleveland, May 26-29. Rev. John J. Flanagan, S.J., 1438 South Grand Blvd., St. Louis 4, Director.

CONNECTICUT STATE MEDICAL SOCIETY, Hartford, April 29-May 1. Dr. Creighton Barker, 160 St. Ronan Street, New Haven, Secretary.

FLORIDA MEDICAL ASSOCIATION, Hollywood, April 27-30. Dr. Samuel M. Day, P. O. Box 1018, Jacksonville, Secretary.

GEORGIA, MEDICAL ASSOCIATION OF, Atlanta-Biltmore Hotel, Atlanta, May 12-14. Dr. David H. Poer, 875 West Peachtree St. N.E., Atlanta, Secretary.

HAWAII TERRITORIAL MEDICAL ASSOCIATION, Honolulu, May 1-4. Dr. I. L. Tilden, 510 S. Beretania St., Honolulu 13, Secretary.

IDAHO STATE MEDICAL ASSOCIATION, Sun Valley, June 15-18. Dr. Robert S. McKeon, 305 Sun Bldg., Boise, Secretary.

ILLINOIS STATE MEDICAL SOCIETY, Hotel Sherman, Chicago, May 13-15. Dr. Harold M. Camp, 224 South Main St., Monmouth, Secretary.

IOWA STATE MEDICAL SOCIETY, Des Moines, April 28-30. Dr. Allan B. Phillips, 406 Sixth Avenue, Des Moines 9, Secretary.

KANSAS MEDICAL SOCIETY, Town House, Kansas City, April 27-May 1. Dr. Dale D. Vermillion, 512 New England Bldg., Topeka, Secretary.

LOUISIANA STATE MEDICAL SOCIETY, Shreveport, April 28-30. Dr. C. Grenes Cole, 1430 Tulane Ave., New Orleans 12, Secretary.

MARYLAND, MEDICAL AND CHIRURGICAL FACULTY OF THE STATE OF, Baltimore, April 28-30. Dr. George H. Yeager, 1211 Cathedral St., Baltimore 1, Secretary.

MASSACHUSETTS MEDICAL SOCIETY, Hotel Statler, Boston, May 20-22. Dr. H. Quimby Gallupe, 22 Fenway, Boston 15, Secretary.

MINNESOTA STATE MEDICAL ASSOCIATION, Minneapolis, May 26-28. Dr. B. B. Souster, 496 Lowry Medical Arts Bldg., St. Paul 2, Secretary.

MISSISSIPPI STATE MEDICAL ASSOCIATION, Jackson, May 13-15. Mr. Roland B. Kennedy, 508 First Federal Bldg., Jackson, Executive Secretary.

NATIONAL TUBERCULOSIS ASSOCIATION, Copley Plaza and Statler Hotels, Boston, May 26-30. Mr. Kemp D. Battle, 1790 Broadway, New York 19, Secretary.

NEBRASKA STATE MEDICAL ASSOCIATION, Cornhusker Hotel, Lincoln, May 12-15. Dr. R. B. Adams, 1315 Sharp Bldg., Lincoln 8, Secretary.

NEW JERSEY, MEDICAL SOCIETY OF, Haddon Hall, Atlantic City, May 19-21. Dr. Marcus H. Greifinger, 315 West State St., Trenton 8, Secretary.

NEW MEXICO MEDICAL SOCIETY, Carlsbad, May 8-10. Dr. L. G. Rice Jr., 221 West Central Ave., Albuquerque, Secretary.

NEW YORK, MEDICAL SOCIETY OF THE STATE OF, Hotel Statler, New York, May 12-16. Dr. Walter P. Anderton, 292 Madison Ave., New York 17, Secretary.

NORTH CAROLINA, MEDICAL SOCIETY OF THE STATE OF, Hotel Carolina, Pinehurst, May 5-7. Dr. Millard D. Hill, 203 Capitol Club Bldg., Raleigh, Secretary.

OGDEN SURGICAL SOCIETY, Orpheum Theater, Ogden, Utah, May 21-23. Dr. George M. Fister, Ogden, Utah, President.

OHIO STATE MEDICAL ASSOCIATION, Cleveland, May 20-22. Mr. Charles S. Nelson, 79 East State St., Columbus 15, Executive Secretary.

OKLAHOMA STATE MEDICAL ASSOCIATION, Oklahoma City, May 19-21. Mr. R. H. Graham, 1227 Classen St., Oklahoma City, Executive Secretary.

RHODE ISLAND MEDICAL SOCIETY, Providence, May 6-8. Dr. Morgan Cutts, 106 Francis St., Providence 3, Secretary.

SOCIETY FOR INVESTIGATIVE DERMATOLOGY, Hotel Sherman, Chicago, June 7-8. Dr. Herman Beerman, 255 South 17th St., Philadelphia 3, Secretary.

SOCIETY FOR PEDIATRIC RESEARCH, Old Point Comfort, Va., May 5-6. Dr. Sydney S. Gellis, 300 Longwood Ave., Boston 15, Secretary.

SOCIETY FOR VASCULAR SURGERY, Chicago, June 8, Dr. George D. Lilly, 331 Ingraham Bldg., Miami 32, Fla., Secretary.

SOCIETY OF AMERICAN BACTERIOLOGISTS, Hotel Statler, Boston, April 27-May 1. Dr. Henry W. Scherp, 260 Crittenden Blvd., Rochester 20, N. Y., Secretary.

SOCIETY OF BIOLOGICAL PSYCHIATRY, Hotel Claridge, Atlantic City, N. J., May 11. Dr. George N. Thompson, 1136 West Sixth St., Los Angeles 17, Secretary.

SOUTH CAROLINA MEDICAL ASSOCIATION, Ocean Forest Hotel, Myrtle Beach, May 13-15. Dr. N. B. Heyward, 120 West Cheves St., Florence, Secretary.

SOUTH DAKOTA STATE MEDICAL ASSOCIATION, Sioux Falls, May 18-20. Dr. L. J. Pankow, 302 First National Bank Bldg., Sioux Falls, Secretary.

SOUTHERN OREGON MEDICAL SOCIETY, Roseburg, May 13. Dr. F. C. Adams, 1435 Esplanade St., Klamath Falls, Secretary.

TEXAS MEDICAL ASSOCIATION, Dallas, May 4-7. Dr. Sam N. Key Sr., 700 Guadalupe St., Austin 3, Secretary.

THE ENDOCRINE SOCIETY, Palmer House, Chicago, June 5-7. Dr. Henry H. Turner, 1200 North Walker St., Oklahoma City 3, Secretary.

WYOMING STATE MEDICAL SOCIETY, Nobel Hotel, Lander, June 5-7. Dr. Glenn W. Koford, 2020 Carey Ave., Cheyenne, Secretary.

INTERNATIONAL

AUSTRALASIAN MEDICAL CONGRESS, Melbourne Victoria, Australia, Aug. 22-30. Dr. C. H. Dickson, Medical Society Hall, 426 Albert St., East Melbourne, Victoria, Australia, General Secretary.

COMMONWEALTH AND EMPIRE HEALTH AND TUBERCULOSIS CONFERENCE, Central Hall, London, England, July 8-13. Dr. J. H. Harley Williams, Tavistock House North, Tavistock Sq., London, W.C.1, England, Secretary General.

CONGRESS OF THE INTERNATIONAL DIABETES FEDERATION, Leyden, Netherlands, July 7-12. Dr. F. Gerritzen, 33, Prinsegracht, The Hague, Netherlands, Secretary.

EUROPEAN CONGRESS OF CARDIOLOGY. University of London, Bloomsbury, W.C.1, England, Sept. 10-12. Dr. K. Shirley Smith, 35 Wimpole St., London, W.1, England, Secretary.

EUROPEAN SOCIETY OF CARDIOVASCULAR SURGERY, Strasbourg, France, Oct. 3-4. Sir James Learmonth, Department of Surgery, University New Buildings, Edinburgh 8, Scotland.

INTERAMERICAN CARDIOLOGICAL CONGRESS, Buenos Aires, Argentina, Aug. 31-Sept. 7. Dr. Blas Moia, Larrea 1132, Buenos Aires, Argentina, Secretary-General.

INTER-AMERICAN CONGRESS OF PUBLIC HEALTH, Havana, Cuba, Sept. 27-Oct. 1. Pan-American Sanitary Bureau, 2001 Connecticut Ave., Washington, D. C.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Mexico City, Mexico, Nov. 2-8. Dr. Guido Torres Martinez, Marsella No. 11, Mexico, D.F., Secretary-General.

INTERNATIONAL COLLEGE OF SURGEONS, Madrid, Spain, May 20-24. Dr. Max Thorek, 850 West Irving Park Road, Chicago, Ill., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF BIOCHEMISTRY, Paris, France, July 21-27. Prof. Jean Courtois, 4, Avenue de l'Observatoire, Paris 6e, France, Secretary.

INTERNATIONAL CONGRESS OF COMPARATIVE PATHOLOGY, Madrid, Spain, May 4-11. Prof. Carda-Aparici, Calle Fernando VI.8, Madrid, Spain, Secretary.

INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY, London, England, July 21-26. Dr. Gordon B. Mitchell-Heggs, 5, Lisle St., London, W.C.2, England, General Secretary.

INTERNATIONAL CONGRESS OF DIETETICS, Royal Tropical Institute, Amsterdam, The Netherlands, July 7-11. Miss Diane J. Ten Haaf, Educational Bureau of the Nutritional Council, 42 Koninginnegracht, The Hague, Netherlands, General Secretary.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Rio de Janeiro, Brazil, Aug. 24-30. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, Executive Secretary.

INTERNATIONAL CONGRESS OF HAEMATOLOGY, Mar del Plata, Argentina, Sept. 21-26. Dr. Carlos Reussi, Anchorena 1710, Buenos Aires, Argentina, Secretary.

INTERNATIONAL CONGRESS OF HEALTH TECHNICIANS, Palais de la Mutualite, Paris, France, June 9-14. Secretariat General, 6 Square Desaix, Paris XV°, France.

INTERNATIONAL CONGRESS OF THE HISTORY OF MEDICINE, Nice-Cannes, France, and Monaco, Sept. 8-18. Dr. F. A. Sondervorst, 124 Avenue des Allies, Louvain, Belgium, Secretary-General.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Friends House, London, N.W.1, Eng. Sept. 15-18. Sir Harold Boldero, 12 Pall Mall East, London, S.W.1, England, Secretary.

INTERNATIONAL CONGRESS ON MEDICAL RECORDS, London, England, Sept. 7-12. Miss Gwen Perkins, 120 C Street S.E., Washington, D. C., Chairman.

INTERNATIONAL CONGRESS OF MEDICINE AND SPORT, Paris, France. May 29-June 1. Prof. Chailley-Bert, 1 rue Lacretelle, Paris 15°, France, Chairman.

INTERNATIONAL CONGRESS ON NEUROPATHOLOGY, Rome, Italy, Sept. 8-13. Dr. Armando Ferraro, 722 W. 168th St., New York, N. Y., U. S. A., Secretary General.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, London, England, July 14-19. Dr. A. C. Boyle, 45, Lincoln's Inn Fields, London, W.C.2, England, Hon. Secretary.

INTERNATIONAL CONGRESS OF PHYSIOPATHOLOGY OF ANIMAL REPRODUCTION AND ARTIFICIAL INSEMINATION, Copenhagen, Denmark, July 7-10. Prof. Ed. Sorensen, The Royal Veterinary and Agricultural College, Bülowsvej 13, Copenhagen V, Denmark.

INTERNATIONAL CONGRESS OF UROLOGY, The Waldorf-Astoria, New York, N. Y., U. S. A., Sept. 15-18. Dr. John A. Taylor, 2 East 54th St., New York, N. Y., U. S. A., Secretary-General.

INTERNATIONAL SOCIETY OF GEOGRAPHIC PATHOLOGY, Liège, Belgium, July 15-18. Dr. Fred C. Roulet, Habelstr. 24, Basel, Switzerland, Secretary General.

INTERNATIONAL UNION AGAINST TUBERCULOSIS, Rio de Janeiro, Brazil, Aug. 24-27. Prof. Etienne Bernard, 66 Blvd. St. Michel, Paris 6e, France, Secretary-General.

NEURORADIOLOGIC SYMPOSIUM, Stockholm, Sweden, Sept. 17-20. Docent Ake Lindbom, Symposium Neuroradiologicum, Serafimerlasarettet, Stockholm K., Sweden, Secretary.

PAN-AMERICAN CONGRESS OF GASTROENTEROLOGY, Mexico City, D.F., May 11-17. Dr. R. Flores-Lopez, Calle Dr. Balmis, No. 148, Mexico City, D.F., Secretary.

WORLD MEDICAL ASSOCIATION, Athens, Greece, Oct. 12-16. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary General.

DEATHS

McCoy, George Walter ✦ Washington, D. C., since 1916 a member of the Council on Pharmacy and Chemistry of the American Medical Association, died April 2, aged 75, of coronary thrombosis. Dr. McCoy was born in Cumberland Valley, Pa., June 4, 1876. He was graduated from the University of Pennsylvania School of Medicine, Philadelphia in 1898 and two years later joined the U. S. Marine Hospital Service, now the U. S. Public Health Service. He served first as assistant surgeon, becoming surgeon in 1913 and a medical director in 1930. He retired from the Public Health Service in 1940 after a long and distinguished career. Dr. McCoy was in charge of the U. S. Plague Laboratory in San Francisco from 1908 to 1911; and from 1911 to 1915, when director of the U. S. Leprosy Investigation Station, he concurrently served as sanitary adviser to the Hawaiian Government. In 1915 he became director of the Hygienic Laboratory of the Public Health Service, now known as the National Institute of Health. On concluding his service with the institute in 1937, Dr. McCoy became engaged in epidemiologic studies in leprosy and in 1938 became director of the department of preventive medicine and public health at the Louisiana State University School of Medicine, New Orleans, serving until 1947 when he became professor emeritus. In 1945-1946 he was acting dean at the university.

Dr. McCoy was a member of the American Society of Tropical Medicine, American Association of Pathologists and Bacteriologists, Association of Military Surgeons of the United States, American Public Health Association, Philadelphia Pathological Society, California Academy of Medicine, Association of American Physicians, and the American College of Physicians. He was an honorary member of Delta Omega and in 1935 president of the Washington (D. C.) Academy of Science. For many years he was an honorary vice-president of the American Mission to Lepers. He was also a diplomate of the National Board of Medical Examiners and since 1920 had been a member of the U. S. Pharmacopeia Revision Committee. As a member of the Committee for the Protection of Medical Research of the American Medical Association for more than 20 years he provided congressional committees with information on bills introduced by antivivisectionists and antivaccinationists. These presentations did much to obviate the hazards of legislation that would obstruct the progress of scientific medicine.

The study of leprosy was a lifelong interest of Dr. McCoy. While his contributions to the literature included numerous papers on bacteriology and public health subjects, they reflected a special interest in plague and leprosy. In 1933 he was a member of a board to study the existing facilities for the care and treatment of leprous persons in Hawaii, and, in 1937, on his retirement as director of the National Institute of Health, he was assigned by the Public Health Service to make a study of the disease in the Continental United States and the island possessions. In 1937 he delivered the second Charles Franklin Craig Lecture at the American Society of Tropical Medicine on "The History of Leprosy in the United States." Dr. McCoy had represented his country on the Permanent Standards Commission of the Health Section of the League of Nations from 1922 to 1937, and later served as a member of an advisory committee to the National Foundation for Infantile Paralysis. In 1931 Dr. McCoy was awarded the Sedgwick Memorial Medal of the American Public Health Association.

Ralston, William Wallace ✦ Houston, Texas; born in Hempstead, Texas, June 8, 1875; University of Texas School of Medicine, Galveston, 1899; veteran of the Spanish-American War and World War I; past president of the Harris County Medical Society; one of the founders and past president of the Texas Society of Ophthalmology and Otolaryngology; member of the House of Delegates of the American Medical Association in 1920; served as councilor of the Ninth District of the State Medical Association of Texas; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; consulting ophthalmologist, Methodist and Hermann hospitals; one of the founders and ophthalmologist, Houston Eye, Ear and Throat Hospital, where he died Nov. 3, aged 76, of cerebral hemorrhage.

Williams, Charles Mallory ✦ Stonington, Conn.; born Oct. 6, 1872; Columbia University College of Physicians and Surgeons, New York, 1898; served as professor of dermatology and syphilology at the New York Post-Graduate Medical School and Hospital, Columbia University; formerly professor of diseases of the skin at the University of Vermont College of Medicine in Burlington; specialist certified by the American Board of Dermatology and Syphilology; member of the American Dermatological Association; served during World War I; president of the medical board from 1928 to 1934 and attending physician from 1920 to 1934, New York Skin and Cancer Hospital; formerly consulting dermatologist, Memorial Hospital; died Nov. 12, aged 79.

Sheahan, William Lawrence, New Haven, Conn.; College of Physicians and Surgeons, Baltimore, 1912; formerly clinical instructor of ophthalmology at Yale University School of Medicine; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; served during World War I; member of the American Medical Association and the American Academy of Ophthalmology and Otolaryngology; twice served on the board of aldermen; affiliated with Grace Hospital and the Hospital of St. Raphael, where he died Dec. 16, aged 64.

Allen, Maurice Linsey ✦ Cleveland; Starling-Ohio Medical College, Columbus, 1913; on the courtesy staffs of Huron Road, St. Luke's, and Booth Memorial hospitals; on the staff of the Glenville Hospital; died in Lakeside Hospital Jan. 20, aged 61.

Anderson, William Jefferson ✦ Meridian, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1902; member of the American Academy of General Practice; died Dec. 19, aged 79.

Bayley, Alvin Jay ✦ Colonel, U. S. Army, Glendale, Calif.; University of California Medical School, Los Angeles, 1912; served during World War I; enterd the regular army in April 1917; retired Nov. 30, 1946; died in Los Angeles Jan. 5, aged 64, of pneumonia.

Biles, James David ✦ Sumner, Miss.; Louisville (Ky.) Medical College, 1898; past president of the Clarksdale and Six Counties Medical Society; vice-president of the Bank of Sumner; for many years surgeon for the Illinois Central Railroad; died in Baptist Hospital, Memphis, Tenn., Dec. 21, aged 79, of congestive heart failure.

Billings, Alva Edgar, Topeka, Kan.; University Medical College of Kansas City, Mo., 1909; member of the American Medical Association; served during World War I; died in the Veterans Administration Hospital, Knoxville, Iowa, Jan. 16, aged 71, of pneumonia.

Boleyn, E. Sydney, Stillwater, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1894; secretary of the Washington County Medical Society; on the staff of the Lakeview Memorial Hospital, died Dec. 23, aged 87, of coronary thrombosis.

Cousins, William Lewis, Portland, Maine; University of Pennsylvania Department of Medicine, Philadelphia, 1894; past president of the Cumberland County Medical Society; fellow of the American College of Surgeons; member of the New England Surgical Society; served during World War I; consulting surgeon, Maine General Hospital; died Feb. 16, aged 81, of hemiplegia.

✦ Indicates Fellow of the American Medical Association.

Gordon, Clifford Myota, Los Angeles; Howard University College of Medicine, Washington, D. C., 1927; died Jan. 22, aged 51, of bronchogenic carcinoma.

Gorson, Samuel Francis ⊕ Atlantic City, N. J.; Jefferson Medical College of Philadelphia, 1915; examining physician for the New Jersey Civil Service Commission; affiliated with Atlantic City Hospital, where he died Jan. 26, aged 59, of acute coronary occlusion.

Gottlieb, Bernard Norman ⊕ Brooklyn; Medical College of Virginia, Richmond, 1925; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the International College of Surgeons; served during World War I; on the staffs of the Cumberland and Prospect Heights hospitals; died in Mount Sinai Hospital, New York, Jan. 30, aged 51, of uremia.

Gravatt, Arthur B., Ellerson, Va.; University College of Medicine, Richmond, 1909; served as county coroner; for many years a surgeon for the Chesapeake and Ohio Railroad; served on the staffs of the Stuart Circle Hospital and Retreat for the Sick in Richmond; died Jan. 2, aged 67, of cerebral hemorrhage.

Haft, Henry Harris ⊕ Syracuse, N. Y.; Syracuse University College of Medicine, 1917; clinical professor of medicine at his alma mater; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; served during World Wars I and II; on the staff of the Hospital of the Good Shepherd, Syracuse University; died Jan. 23, aged 60, of leukemia.

Hagmeier, Otto Charles, Seaside, Ore.; College of Physicians and Surgeons, Baltimore, 1906; member of the American Medical Association; served during World War I; appointed to the state board of health in 1945, later reappointed, and in 1951 served as vice-president and was elected president in January of this year; affiliated with Columbia Hospital in Astoria and Seaside General Hospital; died Jan. 11, aged 73, of carcinoma.

Hedback, Axel Emanuel ⊕ Minneapolis; University of Minnesota College of Medicine and Surgery, Minneapolis, 1897; past president of the Hennepin County Medical Society; formerly member of the state board of health; affiliated with the Swedish Hospital; editor emeritus of *Modern Medicine,* editor of *Geriatrics,* and on the board of editors of *The Journal Lancet;* died Dec. 31, aged 77, of cerebral hemorrhage and cerebral arteriosclerosis.

Hinkson, John Ernest, Lansing, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1895; died in Ypsilanti Dec. 29, aged 81, of arteriosclerotic heart disease.

Houston, Hal Edward ⊕ Murray, Ky.; Vanderbilt University School of Medicine, Nashville, 1935; certified by the National Board of Medical Examiners; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; past president of the Southwestern Medical Association; served during World War II; affiliated with Houston McDavitt Clinic; died in Barnes Hospital, St. Louis, Jan. 14, aged 40, of burns suffered in a fire that destroyed his home.

Hutchings, Ernest Hughs, Sparta, Ga.; University of Georgia Medical Department, Augusta, 1913; died in Columbia, S. C., Dec. 2, aged 65, of cerebral hemorrhage.

Johnson, Hans ⊕ Kerkhoven, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1904; died in Abbott Hospital, Minneapolis, Jan. 21, aged 70, of injuries received in an automobile accident.

Jones, Charles W., Olathe, Kan.; Keokuk (Iowa) Medical College, 1896; veteran of the Spanish-American War and World War I; past president of the Johnson County Medical Society; member of the state board of medical registration and examination; at one time county coroner; on the staff of St. Mary's Hospital in Kansas City, Mo.; formerly director of the First National Bank; died Jan. 28, aged 76, of heart disease and cancer.

La Force, Edward Francis ⊕ Burlington, Iowa; Rush Medical College, Chicago, 1900; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Otolaryngology; died Jan. 22, aged 78, of coronary thrombosis.

Longfellow, Charles Fay, Bloomfield, N. J.; Jefferson Medical College of Philadelphia, 1904; member of the Association for the Study of Internal Secretions; president of the G. W. Carnrick Company in Newark, where he had been vice-president and scientific director and general director of scientific personnel; died Jan. 30, aged 69, of hypertension and arteriosclerosis.

McCabe, William Michael, Nashville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1903; member of the American Medical Association; fellow of the American College of Surgeons; served on the faculty of his alma mater; at one time superintendent of the Tennessee Home Training School for Feebleminded Persons in Donelson, and medical superintendent and surgeon at Nashville City Hospital; formerly associated with Central State Hospital, and the State Prison; died Jan. 3, aged 70.

McNeil, Albert Gordon ⊕ River Forest, Ill.; Bennett Medical College, Chicago, 1912; affiliated with Oak Park (Ill.) Hospital; died Feb. 10, aged 69, of aplastic anemia.

McVay, Lewis Clark ⊕ Phoenix, Ariz.; St. Louis University School of Medicine, 1936; specialist certified by the American Board of Obstetrics and Gynecology; affiliated with Good Samaritan and St. Joseph's hospitals; died Jan. 24, aged 42, of coronary thrombosis.

Macaulay, Evan McLean, Wausau, Wis.; (licensed in Wisconsin in 1899); formerly medical director of Mount View Sanatorium; died Dec. 4, aged 78, of carcinoma of the urinary bladder.

Maes, Charles Gerald ⊕ Kimberly, Wis.; Milwaukee Medical College, 1907; first village president; past president of the staff of St. Elizabeth Hospital in Appleton; died Jan. 8, aged 86, of congestive heart failure.

Merrow, Llewella Maria, Elyria, Ohio; University of Michigan Homeopathic Medical School, Ann Arbor, 1905; died Dec. 16, aged 77, of carcinoma of the stomach.

Miles, May Sallie, Greensboro, N. C.; Laura Memorial Woman's Medical College, Cincinnati, 1898; past president of the Guilford County Medical Society; died in Guilford County Sanatorium in Jamestown Feb. 7, aged 81, of carcinoma of the lungs.

Nason, John Blaisdell ⊕ Tyrone, Pa.; Rush Medical College, Chicago, 1894; served during World War I; for many years chairman of the board of the First Blair County National Bank; died Nov. 30, aged 80, of acute myocardial insufficiency.

O'Leary, Francis Thomas, Logansport, Ind.; University of Nashville (Tenn.) Medical Department, 1899; member of the American Medical Association; died Jan. 22, aged 77, of coronary occlusion.

Owens, Robert Lee, Hockley, Texas; Hospital College of Medicine, Louisville, Ky., 1906; member of the American Medical Association and the Colorado State Medical Society; served during World War I; died in Lubbock Nov. 22, aged 71, of adenocarcinoma of the prostate.

Parker, Ernest Eugene, Oxford, Ind.; Kansas City (Mo.) Homeopathic Medical College, 1901; member of the American Medical Association; served during World War I; formerly county health officer; on the courtesy staff, St. Elizabeth Hospital, where he died Feb. 9, aged 77, of carcinoma of the prostate and peritonitis.

Parker, Gaston C., Chicago; Chicago College of Medicine and Surgery, 1915; member and past president of the staff of Walther Memorial Hospital; chief surgeon of the Chicago Tunnel Company; member of the American Medical Association; died in St. Luke's Hospital Jan. 19, aged 68, of pulmonary embolism and pyelitis.

Parrish, Bert Byrd, Kirksville, Mo.; Barnes Medical College, St. Louis, 1909; died Dec. 20, aged 65, of coronary thrombosis.

Parsons, William Floy, Fort Worth, Texas; Baylor University College of Medicine, Dallas, 1932; fellow of the American College of Surgeons; awarded a Bronze Star during his service in World War II; consultant in surgery, St. Joseph's, Harris, All Saints, and Pennsylvania Avenue hospitals; died Jan. 31, aged 53.

Phippen, Hardy ✦ Salem, Mass.; Harvard Medical School, Boston, 1889; fellow of the American College of Surgeons; member of the New England Surgical Society; surgeon on the advisory staff, Salem Hospital, where he died Jan. 7, aged 89, of arteriosclerotic heart disease.

Pickard, Matthew W., Kerrville, Texas; Kansas City (Mo.) Medical College, 1898; member of the American Medical Association, Industrial Medical Association, and the Missouri State Medical Association; fellow of the American College of Surgeons; died Jan. 1, aged 77.

Pitman, James Fling, Lake City, Fla.; Atlanta College of Physicians and Surgeons, 1913; specialist certified by the American Board of Radiology; member of the Radiological Society of North America, American Medical Association, and the American College of Radiology; past president of the Columbia County Medical Society and the Florida Radiological Society, of which he had been treasurer; served during World War I; affiliated with Veterans Administration Hospital; died Jan. 31, aged 61, of adenocarcinoma.

Pomerene, Myron B., Millersburg, Ohio; Hospital College of Medicine, Louisville, 1902; died Feb. 18, aged 75.

Poole, Charles Judson ✦ Tucson, Ariz.; Barnes Medical College, St. Louis, 1900; member of the Illinois State Medical Society; veteran of the Spanish-American War and World War I; formerly practiced in Mt. Vernon, Ill.; died Nov. 14, aged 77, of lobar pneumonia.

Powers, Edward Emmett ✦ Rome, N. Y.; University of Buffalo School of Medicine, 1912; fellow of the American College of Surgeons; past president of the Oneida County Medical Society; surgeon, Rome Hospital and Murphy Memorial Hospital; consulting surgeon, Oneida County Hospital and Rome State School; died Jan. 9, aged 64.

Ross, George William ✦ Watseka, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; past president of the Iroquois County Medical Society; served as mayor; for many years a member of the high school board; president of the Watseka Public Library; affiliated with Iroquois Hospital; served during World War I; vice president of Iroquois Federal Savings and Loan Association; died in Guadalajara, Mexico, Feb. 9, aged 68, of coronary thrombosis.

Sandusky, Clarence M. ✦ Jacksonville, Fla.; Louisville (Ky.) Medical College, 1902; member of the Southern Medical Association; physician for the Atlantic Coast Line and Seaboard Air Line Railroads; president of the Title & Trust Company of Florida; died in Jefferson Hospital, Philadelphia, Dec. 29, aged 74, of carcinoma of the thyroid gland.

Sawyer, Harold Paine ✦ Colonel, U. S. Army, retired, Montgomery, Ala.; Johns Hopkins University School of Medicine, Baltimore, 1906; served during World Wars I and II; entered the regular army as a captain Sept. 14, 1920; retired as colonel Nov. 30, 1944; from 1946 to 1950 director of laboratories, state department of health; died Dec. 18, aged 71, of mesenteric thrombosis and acute hemorrhagic pancreatitis.

Schaefer, Theodore A., Baltimore; University of Maryland School of Medicine, Baltimore, 1907; member of the American Medical Association; died in Tilghman Jan. 9, aged 78, of diabetes mellitus and cerebral thrombosis.

Schreuder, Louis S., Seattle; Rush Medical College, Chicago, 1898; also a graduate in pharmacy; died Jan. 2, aged 89, of injuries received in a fall.

Schwartz, Alfred Alexander ✦ New York; Columbia University College of Physicians and Surgeons, New York, 1912; member of the American Academy of Ophthalmology and Otolarngology; specialist certified by the American Board of Otolaryngology; served overseas during World War I; affiliated with Montefiore and Sydenham hospitals; died Jan. 13, aged 60, of a heart attack.

Shonkwiler, Allen Joseph, Rockville, Ind.; Medical College of Indiana, Indianapolis, 1905; died Jan. 10, aged 72, of coronary occlusion.

Shurley, Eugene Reginald, Money, Miss.; Mississippi Medical College, Meridian, 1912; died in Greenwood-Lefiore Hospital in Greenwood Jan. 6, aged 67.

Sinclair, Rosa Munda, Dunsmuir, Calif.; California Medical College, San Francisco, 1902; died in Siskiyou County General Hospital, Yreka, Jan. 5, aged 95, of arteriosclerosis and cerebral hemorrhage.

Snyder, Robert John, Philadelphia; Temple University School of Medicine, Philadelphia, 1944; member of the American Medical Association; served during World War II; on the staff of Nazareth Hospital, where he died Dec. 26, aged 32, of heart disease.

Spears, Benjamin Herman, Brooklyn; Albany (N. Y.) Medical College, 1915; died Nov. 21, aged 59, of coronary thrombosis.

Spotts, Samuel Dale ✦ Philadelphia; Jefferson Medical College of Philadelphia, 1922; fellow of the American College of Surgeons; on the faculty of his alma mater; affiliated with Philadelphia General, St. Joseph's, and Jefferson hospitals; on the courtesy staff of Woman's and Hahnemann hospitals; chief of staff and consulting surgeon, Quakertown Community Hospital in Quakertown; a trustee of Bucknell University in Lewisburg, Pa.; died Feb. 1, aged 56, of carcinomatosis secondary to x-ray burns of the hands.

Stanford, John A., Fort Lauderdale, Fla.; Medical College of the State of South Carolina, Charleston, 1909; member of the American Medical Association; served as president of the First National Bank; died Dec. 27, aged 76, of arteriosclerosis and diabetes mellitus.

Starner, Albert A., Oyster Bay, N. Y.; College of Physicians and Surgeons of Chicago, 1896; formerly practiced in Marion, Ohio, where he was affiliated with the City Hospital; died Jan. 21, aged 82, of paralysis agitans and bronchopneumonia.

Stibbens, Frank Hamilton ✦ Oakland, Calif.; Cooper Medical College, San Francisco, 1903; died Feb. 13, aged 73, of bronchopneumonia of the left lung.

Stull, Henry Tuttle ✦ Chevy Chase, Md.; Temple University School of Medicine, Philadelphia, 1913; specialist certified by the American Board of Radiology; member of the American College of Radiology; on the staff of the Suburban Hospital in Bethesda; served as president of the Temple University Alumni Association; died Dec. 18, aged 66, of coronary occlusion.

Tarr, H. L., Jefferson City, Tenn.; Lincoln Memorial University Medical Department, Knoxville, 1907; died in Baptist Hospital, Knoxville, Jan. 7, aged 70, of heart disease.

Thomas, William Marion H., Macon, Ga.; Meharry Medical College, Nashville, Tenn., 1924; died Dec. 4, aged 56, of coronary thrombosis.

Walton, John Marshall, Decatur, Ga.; University of Georgia Medical Department, Augusta, 1926; member of the American Medical Association; formerly associated with the health department in Atlanta; died Jan. 4, aged 50.

Warner, Raymond Crandall, Geneva, Ohio; Cleveland Homeopathic Medical College, 1910; died Feb. 6, aged 70, of Parkinson's disease.

Weaver, Harry Bishop ✦ Greenville, Mich.; Detroit College of Medicine, 1908; past president of the Ionia-Montcalm Counties Medical Society; served during World War I; on the staff of the United Memorial Hospital; died Jan. 25, aged 70, of coronary thrombosis.

Whitehead, Howard, Columbus, Ohio; Starling Medical College, Columbus, 1893; past president of the Columbus Academy of Medicine; one of the founders and directors of the First Federal Savings & Loan Company; died Nov. 10, aged 83.

Williams, Virgil Gaines, Grantville, Ga.; College of Physicians and Surgeons, Baltimore, 1901; died Dec. 16, aged 75.

Wilson, Thomas Luther ✦ Pittsburgh; Maryland Medical College, Baltimore, 1903; on the staff of St. John's Hospital; died Jan. 14, aged 72, of coronary occlusion.

GOVERNMENT SERVICES

ARMY

Pediatric Clinic in Combat Zone.—The first pediatric clinic ever to be established in a combat zone is claimed by X Corps civil affairs officers in Korea. Staffed by qualified pediatricians on active duty, the clinic is held Wednesday afternoons at the X Corps Civilian Hospital. Lt. Comdr. Arvin T. Henderson of Ridgeville, Ind., commanding officer of Medical Company A, First Marine Division hospital, is in charge of the clinic. Treatment for many of the children will be on a weekly "outpatient" basis until exact diagnoses can be made. Patients in serious condition are immediately hospitalized. An officer said "As long as we have empty beds and a light patient load, we can aid our civilian friends at no expense to the Army, using medicines purchased with United Nations Civil Assistance Command, Korea funds."

NAVY

First Aid Program Completed.—The Secretary of Defense in March, 1951, directed the military activities in the District of Columbia to train at least 10% of their personnel in first aid procedures. In compliance with this request the Bureau of Medicine and Surgery, in cooperation with the Navy Department Provost Marshal's Office, organized first aid training courses in the Washington area buildings in which the Navy Department is the major tenant. Nineteen Naval Hospital Corpsmen from Naval medical activities of the area served as instructors. This training program was completed on Feb. 15, 1952, at which time 2,995 individuals had been trained in first aid procedures.

DEPARTMENT OF DEFENSE

Dr. Casberg Succeeds Dr. Lovelace as Chairman.—Secretary of Defense Lovett has announced the resignation of Dr. W. Randolph Lovelace II, as chairman of the Armed Forces Medical Policy Council, and the appointment of Dr. Melvin A. Casberg, vice-chairman of the council, as Dr. Lovelace's successor. Dr. Lovelace stated that his responsibilities in connection with the Lovelace Clinic at Albuquerque, N. M., and with the Lovelace Foundation for Medical Education and Research required his return to private practice. Dr. Casberg, prior to his appointment as vice-chairman of the council in January, 1952, was dean of the St. Louis University School of Medicine. The Armed Forces Medical Policy Council develops and establishes uniform or joint programs in the Army, Navy, and Air Force medical services. The chairman serves as the Secretary of Defense's advisor on medical matters.

Institute of Pathology.—An exhibit tracing 90 years of the history of the Armed Forces Institute of Pathology, formerly the Army Medical Museum, will be opened on May 21, the anniversary of its establishment, in the Medical Museum, 9th and Independence Ave., S. W., Washington, D. C., and will remain on display for six months. Surgeon John H. Brinton, the first curator, toured the battlefields of the Civil War to collect material for the museum and the medical history of the war. On display will be relics of Major Walter Reed, who was curator of the museum when he engaged in his work on yellow fever, and Major F. F. Russell (now brigadier general, ret.) who gave the first immunizing injections in the army against typhoid to volunteers from the museum staff. Other exhibits will show developments in medical illustration through the years, the American Registry of Pathology, which plays an important role in both military and civilian medicine, modern museum techniques, and present day laboratory methods.

When Surgeon General Hammond established the Army Medical Museum in 1862, he envisoned a means of collecting material for research and study to improve the knowledge of Army doctors and aid in their efforts to conquer diseases and injuries incident to war. Today the Armed Forces Institute of Pathology is a central laboratory for diagnosis, research, and instruction for the Navy, Air Force, Veterans Administration, and other federal agencies as well as for the Army. The museum is open to the public.

PUBLIC HEALTH SERVICE

Consultation Laboratory Services.—A part of the program of the Communicable Disease Center, Public Health Service, are the laboratory services. Twelve laboratories perform these services. Consultation services are provided for performance of tests that the state and territorial laboratories cannot offer; for study of organisms presenting problems in identification and evaluation, and for assistance in the solution of other laboratory diagnostic problems.

Ten of the laboratories are located at Chamblee, Ga., and provide services in diphtheria, streptococcus, tuberculosis, enteric bacteriology, special bacteriology (for leptospiral infections and identification of isolated organisms other than those referable to specific laboratory units) mycology, serology, intestinal parasites, blood parasites, and medical entomology. The virus and rickettsia laboratory is located at Montgomery, Ala., and the laboratory concerned with plague in man and rodents is in San Francisco. Specimens from physicians and private laboratories can be submitted for analysis through state laboratory directors and should be addressed to the appropriate laboratory at U. S. Public Health Service, Communicable Disease Center, P. O. Box 185, Chamblee, Ga.; Virus and Rickettsia Laboratory, Communicable Disease Center, Route 3, Box 436, Federal Drive, Montgomery 5, Ala.; or Medical Officer in Charge, CDC Activities, Bldg. 19, 14th Ave. and Lake St., San Francisco 18.

Fewer Marriage Licenses Issued Last Year.—The marriage license upswing that began in June, 1950, at the start of the Korean War, fell off sharply during the last half of 1951, according to the Public Health Service. The 1,621,159 licenses issued during the entire year of 1951 represented a 4% drop from those issued the year before. The decline in marriage licenses in 1951 was shared by 41 states, with only small increases registered in the remaining 7 states.

Personal.—Dr. E. C. Drescher has been appointed chief of the division of commissioned officers succeeding Dr. Eugene A. Gillis, who has been assigned as consultant to the Lebanese Government to assist in furthering the development of public health services in that country. Dr. Drescher is a member of the National Board of Medical Examiners.

VETERANS ADMINISTRATION

New Hospital Managers.—Dr. Bernard L. Allen, at present manager of the general medical and surgical hospital at Clarksburg, W. Va., will become manager of the general medical and surgical hospital at Manchester, N. H. Dr. Lee H. Schlesinger, chief medical officer of the VA Center at White River Junction, Vt., will become manager of the Clarksburg hospital. Dr. Allen will succeed Dr. George O. Pratt as manager at Manchester. Dr. Pratt recently was made manager of the new VA general medical and surgical hospital at Brooklyn.

Dr. George P. Denny, manager of the West Roxbury, Mass., Veterans Administration Hospital, has been appointed manager of the 949 bed general medical and surgical VA hospital that is now under construction in Boston. The Boston hospital is expected to be ready to accept patients sometime in July.

FOREIGN LETTERS

BRAZIL

Albinism in Brothers.—Dr. Guilherme Curban, in the dermatological service of Prof. Aguiar Pupo, of the University of São Paulo, observed so-called total albinism in two brothers and a sister. Their parents and five other children (four male and one female) do not have this cutaneous anomaly; moreover, none of the other 72 known members of the family have total albinism. The analysis of the family's pedigree, after the Mendelian doctrine, demonstrated that the inheritance of total albinism was caused by a recessive, non-sex-linked gene. In the medical literature, there is a case in which two albino brothers had multiple cutaneous carcinoma, and the albino sister remained free from this disease. As one of the possible causes of the carcinomatous degeneration of the skin of the albino brothers, it was thought that the action of sunlight, to which they were exposed, in their profession, might have an effect, whereas their sister, who was a housekeeper, was not so frequently exposed; however, the action of the sunlight was not sufficient to cause the carcinomatous degeneration, because the four other nonalbino brothers do not have skin cancer, in spite of the fact that they are exposed to as much sunlight as their albino brothers. Two of the nonalbino brothers are almost the same age as the patients and have done country work for a longer time; therefore, they have been exposed to sunlight for a longer time. These facts indicate the necessity of special cutaneous conditions, without which the sunlight does not determine the carcinomatous degeneration, according to Dr. Curban. In his study, it was not possible to determine whether these special cutaneous conditions were represented by the lack of protection against the sunlight consequent to the absence of the skin pigment or if they were determined by a genetic predisposition to cancer.

Congenital Anomalies of the Rectum.—Congenital anomalies of the rectum and anus were studied by Drs. Virgílio Carvalho Pinto, Roberto Vilhena de Morais, and José Pinus. The study was based on a series of 33 cases observed in São Paulo. The authors followed the classification proposed by Ladd and Gross. Of 33 cases, 16 belonged to type 3, 7 to type 1, 6 to type 2, and 4 to type 4. Eleven cases of fistula were found, five in males and six in females. In six cases, there were associated anomalies. Usually, these anomalies are surgically treated, types 1 and 2 usually being easily treated. Type 3, when the rectal pouch is low, should be operated on through the perineum; when the rectal pouch is high, an abdominoperineal operation should be performed. A high colostomy should be performed in patients with a high rectal pouch and abdominal distention as well as in patients with advanced cases. In type 4, the rectal segments should be anastomosed or a high colostomy performed, according to the condition of the patient. The operative mortality was 21.4%. In this series, 28 patients were operated on.

ITALY

Convention on Mental Tests.—Professors Gemelli and Gozzano organized a convention in Milan, in order to review problems connected with mental tests, to clarify the relationships in this field between psychologists and psychiatrists, and to assess misunderstandings and abuses derived from the spread of psychology. Many psychologists, psychiatrists, and teachers from Italy and other countries attended the convention.

Professor Gemelli, president of the Catholic University of Milan, who delivered the opening address, advocated that psychology in Italy be recognized and qualified as a profession as has been done in other countries. He expressed concern for the diffusion of mental tests by the nonscientific press, since the tests lose their value when applied to persons who are already aware of their content and their aims.

Professor Rey, from Geneva, reported on psychological tests in cases of pronounced mental backwardness. The speaker distinguished four levels, decreasing in complexity, in the study of the behavior of persons with delayed mental development. At the first level, the person can solve a test involving speech; at the second, the person can solve the test only by imitating actions effected in his presence and involving use of rudimentary language; at the third level, the person can respond by a primitive adaptive reaction to a remote stimulus; and, at the fourth level, the person can react to stimuli only by direct contact.

Professor Pichot, from Paris, reported on methods of evaluating tests and stressed the so-called discriminating factors that make a comprehensive use of the answers possible. This method attempts to establish a simple formula of application; it is less complicated but not less useful than factor analysis. Professor Pichot mentioned an example in which this method was employed in tests given to distinguish insane persons with organic lesions from those without organic lesions.

Professor Meili, from Bern, spoke on analytic intelligence tests, discussing their division into various types, such as tests with numbers, figures, analogies, blanks, designs, and phrases; he also emphasized the importance of the varying scores that the subject obtains. In this way, more can be revealed about the personality of the person than just the intelligence quotient. Professor Ponzo described the organization and the activities of the Italian Society of Psychologists and Psychiatrists of the International Association, the aim of which is to establish coordination between psychiatry and psychological methods.

Professor Gozzano made a critical analysis of the possible means of cooperation between the psychologist and the psychiatrist and asserted that a beneficial collaboration consists of separate examinations of the patient by the psychologist and the psychiatrist, this to be followed by a discussion between them. He added that one of the main tasks of the committee of which Professor Ponzo spoke is the standardization of the tests.

During a meeting of the convention, a motion picture that the United Nations Educational, Scientific, and Cultural Organization (UNESCO) had released to Professor Fulchignoni was shown. Professor Fulchignoni discussed the possibilities and the advantages of the motion picture as a testing medium and emphasized the role that it can play on the tested person with regard to the elements of (1) darkness, (2) rhythmical movement of succession of the images, (3) the "supernormal luminescence," and (4) the progressive disappearance of the images and the sensations aroused.

Dr. Cesa Bianchi, from Milan, gave a report on the use of mental reagents in the study of old age. All psychological activities are diminished between the ages of 67 and 77 years, but the changes in the person's behavior become more pronounced between the 74th and the 78th years. The speaker's observations were limited to persons in a well-defined community and social class; studies in other environments are more difficult because of the heterogeneity of the population. He concluded that his experiences demonstrated that "maladjustment" is mainly observed between the 74th and 78th years.

New Methods of Antituberculous Vaccination.—Two reports were read at a meeting of the Medicosurgical Society of Pisa concerning a new method of antituberculous vaccination called "multiple microfoci vaccination." The first report was given by Drs. Buonomini and Poli, who gave vaccinations with essential anatuberculin incorporated in special receivers. Results showed that it was possible to obtain, in 100% of the vaccinated persons, an allergic condition that can be detected with the common tuberculin test and also systemic changes that can be detected with the erythrocyte sedimentation reaction, the differential blood count, and the titration of the level of the serum antibodies (hemagglutination and deviation of the complement). The

The items in these letters are contributed by regular correspondents in the various foreign countries.

speakers emphasized the advantages of this new method, which is extremely simple and avoids pain, cicatrices, and unpleasant effects.

The second paper was read by Drs. Buonomini and Santopadre, who reported on additional experiments with the "multiple microfoci vaccination," employing Petragnani's anatuberculin. The results proved that with this method it is possible to cause a definite allergic condition in guinea pigs not unlike that obtained with BCG administered by the same procedure. The allergy to tuberculin is preceded, in the vaccinated animals, by a definite and precise bacterial allergy; both the allergy to tuberculin and the bacterial allergy, once established, last for a long time.

LONDON

Training Deaf Children.—According to *The Lancet,* "the education of the general run of deaf children in this country is a failure" if one accepts the standard that "the aim must be to enable all those of sound mentality to join freely, by speech and speech-reading, in conversation with their social and business associates!" This editorial comment was evoked by a letter to *The Lancet* by Miss Edith Whetnall of the Audiology Unit of the Institute of Otology of the University of London. In the letter, it is pointed out that, although the Education Act of 1944 made provision for the teaching of deaf children from the age of 2 years, the necessary facilities for carrying this into effect are generally lacking. A notable exception is the London County Council, which has four nursery schools for the deaf, which are attended by 89 children. Miss Whetnall points out that the age of 2 years is too late to start training if the best results are to be obtained. Training should begin as soon as a child's deafness is suspected by the mother, which is often at the age of 6 to 9 months. Furthermore, "this training must be given continuously by the parents at home under the supervision of a trained teacher of the deaf." The Audiology Unit of the Institute of Otology is now supervising, in this way, the training of 10 children under the age of 18 months and 65 under the age of 5 years. "It is hoped that many will continue their education in ordinary schools." The value of this early training is that it takes advantage of the normal speech learning period that usually ends at the age of 3 years. If such early training were available, many deaf children would eventually be able to attend ordinary schools. An essential part of this training is the use of hearing-aids, so that the child can listen continuously and not only for a few half-hour periods a week. Modern aids are now available that will fit babies. The additional expense of providing such training facilities, including centers, teachers, and aids, would be more than offset by the saving that would be made in special schools. As the president and chairman of The Deaf Children's Society point out in a letter to *The Times*: "If all those deaf children whose residual hearing is usable could have the benefit of really early training, there would be a lessening in demand for places in special schools for the deaf. This would not only mean that the building programme for additional schools for the deaf could be modified, but should ultimately lead to a reduction in the size of classes in existing schools."

Decline in Diphtheria Immunization.—The figures for diphtheria immunization shows a disquieting fall. In 1950, only 433,000 children under the age of 5 years were immunized, compared with 574,000 in 1949, a drop of 141,000. The lower birth rate accounted for only 34,000 of this figure. The Ministry of Health, therefore, instituted an inquiry into the matter, the result of which is published in the February issue of the *Monthly Bulletin of the Ministry of Health.* The inquiry was based on interviews with 1,254 mothers of children aged 6 months to 5 years and a postal questionnaire to the medical officers of health in the 58 administrative districts in England and Wales in which the selected mothers lived. The official aim for diphtheria immunization in Britain has been that 75% of children should be immunized before their first birthday. This inquiry shows that in May, 1951, only 47% of children aged 9 months to under 1 year had received as much as their first injection. Of the entire group of children aged 9 months to 5 years, only 69% had completed their immunization. Other interesting data revealed by this inquiry show that the proportion of children immunized at clinics had fallen from just over two-thirds in 1947 to about one-half in 1951. The proportion immunized by the family physician had risen correspondingly. Two-thirds of the children were given injections in the arms. This site seems to cause less discomfort than the legs or buttocks. The mothers gave the following reasons for not having their children immunized: they were "too young," "father does not agree," "do not believe in it," "never heard of it," and "not bothered." In only nine instances did the mother give poliomyelitis as the reason for postponing immunization. The mothers least cooperative in immunization were those with several children, those from poorer households, and the less well educated.

Motion Sickness Prevention.—Further data suggesting that scopolamine (hyoscine) hydrobromide is the most effective motion-sickness remedy are presented by Glaser and Hervey *(Lancet,* **1**:490 [March 8] 1952). The experiments were carried out in a large swimming bath with artificial waves; the subjects were 150 soldiers. The preparations used were: *l*-scopolamine hydrobromide, 1 mg.; promethazine (N-[2-dimethylamino-n-propyl] phenthiazine hydrochloride) hydrochloride, 35 mg.; scopolamine hydrobromide, 1 mg., with promethazine hydrochloride, 25 mg.; scopolamine hydrobromide 0.65 mg., with promethazine hydrochloride, 15 mg., scopolamine hydrobromide, 0.65 mg., with promethazine hydrochloride, 15 mg., and mannitol hexanitrate, 50 mg.; and lactose (control). All the preparations containing scopolamine were more effective than promethazine, 35 mg., and 35 mg. of promethazine was no more effective than 25 mg., which was the dose that had been used in a previous experiment. The straight comparison betwen scopolamine hydrobromide, 1 mg. and promethazine, 35 mg., showed that the former protected 92% of 98 men against vomiting and 81% against vomiting and nausea, compared with 64% and 53%, respectively, of 99 men given promethazine. The authors conclude "Except for pethidine, all the likely remedies have been investigated during the last eight years in this country and in North America. No further improvements can be expected except by accident or by a systematic study of basic principles."

Factory Accidents.—The report of the chief inspector of factories for 1950 shows a continued decline in the accident rate per 1,000 employed persons. In spite of an increase of 200,000 workers, there was only a slight increase in the number of accidents, 193,059 compared with 192,982 in 1949. The number of fatal accidents was 799 compared with 722 in 1949. One disturbing feature was that the accidents caused by the cleaning of moving machinery by women and young employees rose by 22.5%. This is taken to indicate lack of proper instruction and discipline. Designers and makers of machinery are criticized for not giving enough thought to the elimination of danger points or to the protection of those using the machines. Eye injuries were still common, approximately 200,000. For the first time since lead poisoning became notifiable, in 1895, no fatal accident occurred. Aniline poisoning reached a record low level, but anthrax was commoner among those handling hides and skins.

Alcoholism.—A new approach to the problem of alcoholism is outlined in "Alcoholism: A Social Problem," a booklet published by the Advisory Council on Alcoholism. Mrs. Marty Mann, chairman and executive director of the National Committee on Alcoholism, New York, is acting as consultant to the council. It is estimated that there are 86,000 chronic alcoholics in England and Wales and that four times this number are suffering from alcoholism in its earlier and less virulent stages. Many of the chronic alcoholics are permanently unemployed, and, of these, a fair proportion are either in prison or mental hospitals. The basis of the campaign is that alcoholism is a disease and that the alcoholic is a sick person who can be helped.

Smallpox.—In view of the under-vaccinated state of Britain, some concern is being aroused in public health circles by an outbreak of variola minor in Lancashire. The first case in which laboratory confirmation was obtained was that of an unmarried woman; the rash appeared on Feb. 1. Until March 8, a total of 80 cases had been reported in the same area. All the early cases were in the direct line of contact, but cases are now being reported that could not be associated with previous ones. So far, there is no report of smallpox in any other part of the country.

An educational campaign is being planned to draw attention to the effects on industrial efficiency and to secure adequate hospital and clinic facilities.

Metabolic and Radioisotope Ward.—At a cost of £12,000, which the hospital has provided from its special funds, a special ward for the study of metabolic disorders and the use of radioisotopes in treatment has just been opened at University College Hospital. It includes two rooms, with three beds in each, two rooms, with one bed in each, a special diet kitchen, research laboratories, and an isotope laboratory, with a "cellar" and an observation room.

NORWAY

Medical Supervision of Industrial Concerns.—A scheme recently endorsed by the Norwegian Medical Association, the Norwegian Employers' Association, and the Norwegian Labor Party was reported on at a meeting of the Norwegian Medical Society in Oslo, by Prof. Axel Ström and Prof. Haakon Natvig, who have taken an active part in promoting it. Under this scheme, clerical and manual workers in various industrial concerns and government services are kept under the close medical supervision of physicians representing the elite of the medical profession. Prof. Natvig has undertaken an analysis of the reports sent in by these physicians in 1948 and 1949 with a view to demonstrating the activities and most important findings of this scheme, which, by the autumn of 1951, was in operation in 540 industrial and other concerns employing many thousands of clerical and manual workers. The triple object of this scheme is to discover hitherto unknown cases of disease, to give advice on health problems, and to learn the frequency of certain diseases and conditions affecting health. The form on which the findings of these physicians were to be entered was drafted so as to yield special information about 19 different groups of diseases or anomalies. The tuberculous diseases, for example, formed one of these groups, and it was noted that, in the course of 37,896 medical examinations in 1949, as many as 500 tuberculous cases were found, and 81 of these patients had not hitherto received medical treatment.

Meinicke's reaction test for syphilis did not require a sample of blood, because the citrated blood taken for the sedimentation-rate test was sufficient for both purposes. All the positive Meinicke reactions were verified by other means, and it was remarkable that the percentage of positive reactions in men fell from 2 in 1948 to 0.8 in 1949. In the same period, the figures for women were 1.4% and 0.74%, respectively. This pronounced fall in so short a time reflected the general fall in the syphilis rate in Norway as well as the measures taken in this section of the community to combat syphilis. Another series of observations concerned absence rates because of illness. This rate was much higher for women than for men, the number of days of absence per year because of illness being 11.4 for men and 17.9 for women. But the average duration of each illness was longer for men than for women, with 11.9 days for the former and 9.4 for the latter. Absence because of tuberculosis accounted for 7.5% of the total absence for male manual workers and 9.2% for male clerical workers, the corresponding figures being approximately half for the two groups of female workers. Absence because of accidents and injury was also twice as great among men as among women.

Formerly, contact between patient and physician was usually made on the initiative of the former, often a tardy initiative. Now, contact between the two is often made on the initiative of the physician, who is trained to detect early signs of disease and who has knowledge of the conditions most likely to promote it. Because it is so new, this scheme has been challenged by persons who have asked questions concerning cost, returns, and the balance between cost and returns. Professor Natvig calculates that the cost per head per year is approximately 20 Norwegian kroner ($3.00). As for the returns, he calculates that among 165,000 persons examined under this scheme, 350 may be found to suffer from tuberculosis, 250 from syphilis, and 110 from cancer, every year. Many other major and minor ailments would also be found. It is almost impossible to calculate in figures, in the coin of the realm, the value of such findings. What is impressive is the discovery that when supposedly healthy persons engaged in full-time occupations are systematically examined by physicians familiar with occupational diseases, between 10 and 15% are found to be in need of medical treatment for some ailment.

Contribution of Sports to the Health of the People.—During the Olympic winter sports games in Norway in February, a series of 35 lectures on sports and health were delivered by selected speakers. Representing the World Health Organization, Dr. Milton I. Roemer warned against the exclusive culture of "stars" and the neglect of the average person, who is apt to be discouraged as he stands idly by, watching the elite. Roemer pleaded for recreational facilities and a moderate form of physical culture for the older age groups. He criticized those teachers who reward scholars for not missing a single hour at school without regarding the possibility that absence on account of ill health may be laudable in certain instances.

In speaking on the same subject, Dr. Karl Evang, head of the health services in Norway, drew attention to some of the less desirable aspects of sports at the present time, such as the use of various injections to stimulate contestants who do not feel at their best at the starting point. He would like to see the health authorities in different countries adopt such measures as the systematic medical control of all active participants in sporting events, the prohibition of certain kinds of sport, the encouragement of forms of sport that are suitable for weaker persons and the promotion of sporting events that depend on team spirit and cooperative action.

Another speaker, Dr. Gunnar Johnson, who has been in charge of the emergency medical service for Oslo for 17 years, said that the accident rate was relatively high among casual participants in sports as compared with well-trained "stars"; hence, he suggested that untrained persons should not be allowed to take part in sporting competitions. Dr. Ervin Mathé of Prague dealt with his experiences in treating 40,000 skiers between 1946 and 1950. He, too, had found that the trained skier was less prone to accidents than the casual skier. Dr. Henrik Seyffarth dealt with functional neuritis in connection with sports, and he suggested that various diagnoses, such as flat feet, could be traced to functional neuritis, which, in turn, may be the result of faulty muscular action and inadequate relaxation.

The Negligible Risk of Superinfection with Tubercle Bacilli.—The thesis recently advanced by Dr. J. Heimbeck that intensive infection of tuberculin-negative persons and superinfection of already infected persons have much to do with the evolution of tuberculosis is severely criticized by Dr. Rolv Höyer Dahl, who is in charge of the large Glittre Sanatorium. In Dahl's opinion, Heimbeck has shown ignorance of statistical techniques in his analysis of his observations. Heimbeck's claim that tuberculosis morbidity was greater among the nurses of Ullevaal Hospital than among the young women in the general population of Oslo is open to the objection that the nurses were under much closer medical supervision than the controls, many of whom may well have suffered from some degree of tuberculosis without their knowledge. Although sputum-positive pulmonary tuberculosis and deaths from tuberculosis are well-defined conditions, tuberculosis morbidity shades off imperceptibly with various degrees, the mildest of which are easily overlooked.

In support of his opinion that the risks of superinfection are negligible, Dahl quotes observations from Glittre Sanatorium, where in 1949 and 1950, a total of 250 patients with cavities were discharged. These patients had been infected between the ages of 15 and 24. In each case, the interval between infection and the appearance of the first cavity was known. This interval was approximately 1 year in 62 patients, 2 years in 46 patients, 3 years in 30 patients, 4 to 5 years in some patients, and 6 to 10 years in still fewer patients. Had superinfection played the serious part allotted to it by Heimbeck, these figures would have shown a more uniform distribution instead of the marked fall from the first year after infection. Dahl concludes that "we can, as far as I see, take the risk of massive infection and superinfection with equanimity. We sanatorium doctors can continue to treat our patients in the same wards. The results are not better in the sanatoriums with only one-bed wards."

CORRESPONDENCE

THE SNOWBOUND "CITY OF SAN FRANCISCO"

Because of the national interest that was shown when the train "City of San Francisco" became snowbound in January in the Sierra Mountains, the only physician aboard this train was asked to report his experiences. His letter follows.—ED.

To the Editor:—The westbound "City of San Francisco" became snowbound the morning of Jan. 13, 1952, in the high Sierra Mountains at Yuba Pass. An unprecedented snowfall had occurred, and shortly before noon the diesel engine of the streamliner was struck by a snow slide that brought the train to an abrupt stop. The snowfall continued for several days and was estimated to be between 14 and 18 feet, with drifts of 20 to 25 feet, in places even higher. During this time the outside temperature was about 20 degrees above zero, and winds between 40 and 50 miles per hour were recorded.

Very little actual concern was felt for the passengers during the first few hours after the stopping of the train; however, medical problems developed rather rapidly.

In the afternoon of Jan. 13, word reached me that the engineer of an eastbound train had been injured that morning and had been transferred to the westbound streamliner for transportation to Sacramento. The report stated that he was in great pain. My services were volunteered to the conductor in charge of the train; however, he explained that, while the report of the injured man was true, apparently he was not in any great pain and did not require any medical attention at that time. Later events substantiated the conductor's opinion. As a result of this, however, the train crew was aware of the fact that a physician was aboard. In a matter of several hours, four nurses aboard the train volunteered to aid in any way. While their services were not required until the following day, they were immediately available.

During the evening of Jan. 13, several members of the train crew sought my aid for a young man in one of the cars. It was reported that the young man was in considerable pain and, if possible, needed immediate help. I saw the patient, who was a man about 30 years old, and he gave a history of tuberculous osteomyelitis of the right humerus and right tibia. He stated that intense pain was present in this area. The patient was perspiring rather profusely and seemed to be quite agitated. He was apparently afebrile, and, while old scars were present, no draining sinuses were seen and there was no localization of pain. No evidence of abscess formation was noted.

It was then apparent that the man was an addict, and the question was asked, "How much and how often?" The answer was, "One half grain of morphine sulfate every three hours." While it is not my practice to carry any emergency drugs on a vacation, on this particular trip I was to accompany a patient and friend of mine to the coast. He had suffered a rather severe coronary lesion about two years ago and about one year ago an acute attack of gallstone colic. Inasmuch as he was in advanced years, I brought with me a few emergency drugs. These consisted of one 30 cc. vial of morphine sulfate, one vial of penicillin powder, 2 million units, and a small amount of acetylsalicylic acid.

It became obvious that the morphine sulfate would be of great help, since the addict was on board. His personal supply had become exhausted. I was fully aware of my responsibility, which under normal circumstances would have prevented me from giving him any morphine; however, under these conditions, I saw no alternative except to maintain him as best I could with a minimum dosage. It was explained to him that he would be given only sufficient morphine to maintain him until he could be evacuated, and then he would be hospitalized. He eagerly accepted these conditions and was given ¼ grain (15 mg.) subcutaneously. Very little effect was noted, and in approximately one-half hour an additional ¼ grain was given. During the entire time we were snowbound, he was given approximately ½ grain (30 mg.) of morphine sulfate every six to eight hours, and, while it did not relieve his withdrawal symptoms, it did control him sufficiently to prevent him from being a major problem to the other passengers. He was kept in a bedroom, where meals, which he rarely ate, were taken to him.

During the evening and night of Jan. 13, the temperature in the cars began to fall because the fuel oil in the diesel engines was exhausted. The lighting system also began to fail, and most of the cars were without light. Early on the morning of Jan. 14, word reached me that a trainman who was on a relief engine just ahead of the streamliner was ill. It was necessary to leave the train and administer aid to this man who, while not seriously ill, was apparently completely exhausted from overwork. The return to the streamliner convinced me that our situation was grave and that certain policies and practices would have to be carried out for the health and safety of passengers and crew.

Immediately on my return to the train, a committee was formed to attempt to establish some sort of policy. The committee consisted of passengers and certain members of the train crew. Complete cooperation between these two groups was accomplished quickly. The available milk supply was appraised, and it was sufficient to last several days, provided it was used for children only. The food supply was appraised, and, by careful management, the dining car stewards were able to provide adequate if not choice meals. Additional food, consisting of baked beans and spaghetti, was brought in later. Owing to the lack of light, which by now had been shut out by the snow that covered the windows in most of the cars, meals were served at 9:00 a. m. and 3:00 p. m. By 4:00 p. m. the cars were quite dark.

After the lighting system failed, it was discovered that two of the pullman cars were equipped with propane generators for recharging the batteries. In the evening of Jan. 14, these generators were put in operation. Early in the evening many of the passengers became ill. The illness was manifest by a mild hysteria, shortness of breath, and some nausea. A few patients with upper respiratory illness had already been seen, and these were isolated and treated with penicillin. The dosage was restricted to 100,000 units instead of the usual 300,000 or 400,000 to conserve the available supply in case a greater emergency developed. At no time did this become a major problem.

It was decided to place all the ill passengers in the cars with the auxiliary lighting. In the morning of Jan. 15, some of these persons became quite ill. This was manifest by intense headache, nausea, and vomiting, incontinence of bowels in a few of the passengers, and unconsciousness in 15 or 20 of them. It was realized at this time that some carbon monoxide from the propane generators located underneath the cars had gained access to the cars. In some cases, passengers had locked their compartment doors, and it was necessary to use an emergency axe to gain admittance. The affected persons were removed from these cars, the upper vestibule doors were opened, and sufficient air change occurred within a short time to allow the passengers to regain consciousness; and, with the exception of a few residual headaches and some nausea, all passengers recovered in a few hours. It was obvious that the amount of carbon monoxide present was not great at any time. Neither the passengers nor the crew showed any sign of cyanosis, and of course no blood specimens could have been taken.

The problem of hysteria never was of any great importance. The train crew and passengers alike accepted their entrapment, and most persons must have felt that eventual help would reach us. There was, however, much confusion as to actual responsibility, and a complete lack of communication produced a feeling of anxiety. False rumors and reports were extremely common, and it was difficult to accept the reports that were true

when means of communication were eventually established. It was indeed unfortunate that none of the passengers carried a portable radio and that the streamliner did not have some sort of radio equipment. False rumors consisted of such things as, "The railroad has abandoned any further rescue attempts," "The Army cannot spare men or equipment—they are busy feeding stranded cattle in Nevada," and "The state highway department will not permit four or five new rotary plows to be used because they are not painted."

It is not difficult to see that with such reports many persons became discouraged and were willing to attempt any sort of rescue by themselves. It became necessary to vigorously oppose any attempt at self-rescue. Of course it would have been impossible to evacuate any passengers during the blizzard. Few could have survived the wind or snow, and, even if they had left the train, there would have been no place to go. With the exception of one person who did leave the train and promptly returned, all other passengers heeded this advice and in general cooperated very well.

The magnitude of the rescue attempt that was occurring could not be realized at that time by either passengers or crew, and it was not until Wednesday morning, Jan. 16, that this became evident. The Southern Pacific Railroad had utilized every piece of available equipment, including rotary plows, relief trains, and all available personnel. This personnel had apparently worked long hours against almost insurmountable odds, and one of the trainmen lost his life in the rescue attempt. The Pacific Gas and Electric Company used their personnel and equipment to the best advantage, and through this effort auxiliary food was supplied on Tuesday, Jan. 15. One of these employees also gave his life in the rescue attempt.

The state highway department of California did a magnificent job of opening a road approximately 6 to 8 miles in length through nearly impassable snow drifts, so that passengers and crew could be evacuated through a single lane to the relief train. There must have been many more examples of heroism and self-sacrifice on the part of hundreds of persons of which we, as passengers, knew nothing. A tremendous lesson of faith in our fellow man is thus learned, and this in any disaster becomes paramount.

The lack of heat caused a great deal of inconvenience; however, by keeping fully clothed and using blankets, sufficient body heat was maintained and no frostbite or other evidence of cold injury occurred.

Personal injuries were held to a minimum by discouraging aimless walking through the train. Most passengers remained either in their seats or in the lounge cars throughout the day and night. Excessive stimulation by alcohol was prevented by closing the bar and discouraging excessive drinking on the part of the passengers who had a private supply. The available gin was used for skin and syringe sterilization.

Civilian disaster occurs with sufficient frequency to formulate the following conclusions. A physician, if present, must accept his responsibilities quickly. Most persons are not impressed by a limited specialty and the title Doctor of Medicine is all they expect. The physician must by reason of his profession be placed in authority, in cooperation with others of authority. Simple public health measures may have to be enforced early in the disaster, such as conservation of food, water, and energy on the part of the crew and passengers alike. Persons with contagious diseases must be isolated quickly to prevent an epidemic. A disease or injury must be diagnosed and treated to the best of one's ability, and frequently improvising of equipment and substitutions of drugs must be made. A physician, by virtue of his profession, is expected to maintain some discipline, to evaluate the extent of the emergency, and to provide adequate if not complete medical service. By his actions and manners he must develop a spirit of confidence in eventual rescue and relief.

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NEW ANTITUBERCULOSIS DRUGS

To the Editor:—The editorial entitled "New Antituberculosis Drugs," which appeared in the March 22 issue of THE JOURNAL, was an excellent summary of the information now available; however, more could have been said concerning the caution necessary in the evaluation of these drugs. I should like to call attention to the last four paragraphs of a statement recently prepared by the American Trudeau Society, the medical section of the National Tuberculosis Association:

"At present there is no reason to believe that the fundamentals of therapy of tuberculosis should be altered in any way when isonicotinic acid hydrazide is employed. Patients receiving the drug should be hospitalized for careful observation. They should be studied in institutions where potential toxic manifestations may be watched for most carefully and where effects upon the course of the underlying tuberculosis may be carefully observed so that suitable alterations of therapy may be initiated when indicated. Routine laboratory precautions should include frequent blood counts and urinalyses, neurologic examinations, and tests for renal and hepatic insufficiency.

"The introduction of a new drug in the therapy of tuberculosis is likely to raise more questions for a few years than it will answer. There is no knowledge at the present time that isonicotinic acid hydrazide or its isopropyl derivative will accomplish more than has been accomplished with streptomycin and PAS. It may prove to be an additional drug of great value. It may be years before its exact contribution to the therapy of tuberculosis can be assessed accurately. A large reservoir of undetected and untreated cases of active tuberculosis exists throughout the United States, and there is every expectation that, in spite of the more effective chemotherapy of tuberculosis currently available, the need for hospitalization in institutions with qualified personnel and adequate laboratory facilities will increase rather than decrease. There is at present no basis for expecting that isonicotinic acid hydrazide, or any other drug available, can safely be counted upon to reduce the duration of hospitalization. Rather, in most instances, at least, it may lead to prolongation of hospital treatment since effective chemotherapy may facilitate desirable forms of therapy not otherwise possible.

"It should be emphasized strongly that, with more numerous effective antituberculous compounds available in the treatment of tuberculosis, more intensive case finding than ever will be indicated. Only through this means can maximum advantage be taken of improvements in therapy.

"After a review of available data on the action of isonicotinic acid hydrazide and its isopropyl derivative upon the tubercle bacillus in vitro, and upon the course of experimental tuberculosis in animals and clinical tuberculosis in man, it may be stated that their demonstrated action, although highly encouraging, appears in no way to alter the basic principles of the treatment of tuberculosis as presently understood. Much more work will need to be done to ascertain the exact place of these drugs in the treatment of the disease. With several carefully coordinated studies in prospect, it is anticipated that further information will accumulate rapidly."

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MEDICAL TOURISTS IN GREAT BRITAIN

To the Editor:—I am writing on behalf of the London Hospital Medical Society, to inquire whether you could furnish the names of any American physicians who might be touring the United Kingdom this year. We would like to be able to invite some of them to come and speak to us at the London Hospital.

In the past we have very much enjoyed the visits of our American colleagues, and we would like to hear more from them this year if possible.

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BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Nurses: Tuberculosis As An Occupational Disease.—The petitioner, a registered nurse, filed a claim for compensation under the occupational disease provisions of the workmen's compensation law, alleging that she had contracted tuberculosis out of and in the course of her employment as a nurse in the Medical College of Virginia Hospital. From an order denying an award of compensation, the petitioner appealed to the Supreme Court of Appeals of Virginia.

Section 65-42 of the Virginia Code defines an occupational disease as a disease arising out of and in the course of the employment but provides that no ordinary disease of life to which the general public is exposed outside of the employment shall be compensable except when it follows as an incident of an occupational disease. Section 65-43 provides that "The following diseases and conditions shall be deemed to be occupational diseases, and even they shall not be so considered unless they are in fact occupational within the meaning of the term occupational disease as defined in the preceding section: . . ." then follows a schedule with 15 numbered paragraphs, none of which lists tuberculosis by name, but paragraph 11 thereof provides as follows: "Infectious or contagious diseases contracted in the course of employment in or in immediate connection with a hospital or sanitarium in which persons suffering from such diseases are cared for and treated. . . ." This was the provision on which the petitioner based her claim.

Tuberculosis is a contagious disease, and, said the court, it is also an ordinary disease of life to which the general public is exposed. If only the provisions of section 65-42 are considered, the conclusion would be necessary that claimant's tuberculosis is not compensable since it did not follow as an incident of occupational disease, but when that section and section 65-43 are considered together, it seems fairly certain that it was not the purpose of the law to exclude from compensation every infectious or contagious disease to which the general public is exposed. Reading the two sections together, we think it was intended to provide that infectious or contagious diseases, including tuberculosis, when contracted under the circumstances stated in paragraph 11, and when in fact occupational as defined in section 65-42, i. e., when arising out of and in the course of employment, as further defined in that section, shall be compensable.

It is clear that the legislature did not intend, by the enactment of the occupational disease law, to provide a general system of health insurance. It provided compensation only for occupational diseases and carefully spelled out what was required to fill that description. It provided that no ordinary disease of life to which the general public is exposed outside of the employment shall be compensable. Certain named diseases were made compensable but only if they arose out of the employment as that term is defined in the law. Certain unnamed diseases, embraced in the general description of infectious or contagious diseases were included, provided (1) they are in fact occupational as defined, (2) they were contracted in the course of employment, (3) in or immediately connected with a hospital or sanitarium, and (4) in which persons suffering from such diseases are cared for and treated. No compensation is provided for infectious or contagious diseases that do not meet those terms. If a contagious or infectious disease not specificially named in the statute is contracted in the course of employment in a factory, in a store, in a restaurant, in a garage, or any other place where men and women are employed, it it not compensable, but treated as one of the ordinary diseases of life to which the general public is exposed outside of that employment. Thus the broad provision of section 65-42 that no ordinary disease of life shall be compensable is qualified and an exception made with respect to infectious or contagious diseases if, but only if, they meet the four requirements stated above.

Among those requirements are that the disease must be contracted in a hospital or sanitarium and that hospital or sanitarium must be one in which persons suffering from that disease are cared for and treated. In its context we think this means a hospital or sanitarium in which persons suffering from such disease are cared for and treated as a general practice or as a business, not one that cares for and treats that disease only in an emergency and not one that would decline to admit one suffering from that disease if he came to be treated only for that disease. If it is desirable to extend the provisions of the act to all hospitals, or even other places of work, where contagious diseases may be contracted as a result of working there, that is the business of the legislature. We must take the statute as we find it, gather the legislative intent from the words used and give effect to the purposes thus ascertained. The Supreme Court of Appeals concluded that the defendant is not a hospital in which tuberculosis is cared for and treated in the sense in which that phrase is used in section 65-43 (11), and accordingly, the order denying an award was affirmed. *Van Geuder v. Commonwealth, 65 S. E. (2d) 565 (Virginia 1951).*

MEDICAL MOTION PICTURES

Integrative Aspects of the Nervous System: 16 mm., color, sound, showing time 57 minutes. Produced in 1950 by the United States Army. Procurable on loan from the Surgeon of the Army Area in which the request originates.

The mechanism by which the nervous system functions has long been vaguely understood, but it has only been in the last few years that experimental work has clarified the issues. This has been mainly in the fields of mathematics and physics. Starting with the hypothesis of reverberating circuits, the action of the neuron circuits has been found to be similar to servomechanisms. Feed-back mechanisms are not new concepts, especially in the fields of radar and anti-aircraft guns. "Scanning" mechanisms are also by no means new, as television can attest.

This excellent film graphically portrays the means by which the nervous system is believed to make use of these well-known devices. Starting with the simple stretch reflex the picture goes on to describe the feed-back mechanism in the nervous system. The manner in which feed-back works is exemplified. In action, it is applied to the function of the cerebellum, basal ganglions, and the reticular area in the midbrain. The mechanism is then related to the clinical aspects of disordered movement, such as is seen in Parkinson's disease and cerebellar lesions.

Experimental methods by which certain postulates were reached are portrayed in animals. Decerebrate rigidity is produced, the vestibulospinal tract is stimulated by means of a stereotaxic apparatus, and the tonic neck reflexes are demonstrated, among other things.

An understanding of feed-back is quickly reached through its graphic portrayal in animated drawings, which, in turn, are supported by verbal explanations. Although this material could probably be assimilated by some persons through reading, there are others who do not have the knowledge of mathematics or physics to make it comprehensible. For such persons the film is invaluable. The film was made under the direction of an authority on mathematics and therefore represents a mature point of view rather than that of an enthusiast.

The showing time is over 50 minutes, but it seems shorter, because the film has obviously been carefully prepared. It is of the utmost teaching value, especially in relation to modern concepts of nervous activity. The film represents a great deal of advanced work in experimental nervous physiology and is recommended for medical students and neurologists. It should make clear to them in a few minutes what would otherwise require hours of laborious reading under a trained instructor.

There are some minor flaws, such as an occasional lack of contrast between the animation and its background, which makes some of the words hard to read. In other places, there are slight defects in lighting.

For those interested in the feed-back mechanism itself and its correlation with the nervous system, this motion picture is highly recommended.

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Otolaryngology, Chicago

55:1-100 (Jan.) 1952

*Calcification in Laryngeal Cartilages. J. H. Vastine II and M. F. Vastine. —p. 1.
Hemorrhage in Nose and Throat. H. P. Harkins.—p. 8.
Rhinoplastic Approach to Certain Rhinological Procedures. L. J. Feit. —p. 12.
Mechanism of Shadow Hearing. K. Tschiassny.—p. 22.
Effects of Oxygen Deprivation upon Structure of Organ of Corti. M. Lawrence and E. G. Wever.—p. 31.
Closure of Tympanic Membrane Perforations by Trichloroacetic Acid Cauterization: Report of Cases. L. A. Adams.—p. 38.
Fibrous Dysplasia of Facial Bones and Paranasal Sinuses. H. Brunner. —p. 43.
Poliomyelitis and Laryngologist. M. W. Simmons.—p. 55.
Hearing Loss in Children with Cleft Palates. J. Sataloff and M. Fraser. —p. 61.
Otitis Media and Complications. B. R. Dysart.—p. 70.

Calcification of Laryngeal Cartilages.—Lateral films of the neck were obtained in five pairs of identical twins. Their ages ranged from 13 to over 70 years. It was found that the deposition of calcium in the laryngeal cartilages is strikingly similar in identical twins. It is reasonable to assume, therefore, that the deposition of calcium in the laryngeal cartilages is hereditarily determined and not influenced by or due to any acquired factor, such as disease, mineral deficiency, or metabolic disturbance. The configuration of the hyoid bones and of the cervical spines is also similar in identical twins. Commenting on these observations the authors say that in a previous report they had presented evidence that the size, shape, and contour of the skeletal system is predetermined. Even the most minute detail of ossification is under the direct influence of the genes. This is evident when a close comparison of the roentgenograms of each of the respective bones of identical twins is made. This amazing similarity in the bony structure may prove to be the most accurate criterion for differentiating homozygotic from dizygotic twins.

A.M.A. Arch. Pathology, Chicago

53:1-102 (Jan.) 1952

Nephrotoxic Globulin Nephritis: I. Course After Single Intravenous Injection. R. W. Lippman, H. U. Marti and D. H. Campbell.—p. 1.
Pathological Changes in Acute and in Protracted Vitamin A Deficiency: Their Prevention by "Lard Factor." H. C. Stoerk, H. Kaunitz and C. A. Slanetz.—p. 15.
*Induction of Thyroid Cancer in Rat by Radioactive Iodine. R. C. Goldberg and I. L. Chaikoff.—p. 22.
Comparison of Aging Processes in Renal and Splenic Arteries in the Negro and White Races. F. P. Handler, J. O. Blache and H. T. Blumenthal.—p. 29.
Cortisone and Matrix Formation in Experimental Scorbutus and Repair Therefrom, with Contributions to Pathology of Experimental Scorbutus. S. B. Wolbach and C. L. Maddock.—p. 54.
Role of Arachnoid Granulation in Development of Meningioma. L. Wolman.—p. 70.
Studies on Methods of Staining Islet Cells of Pancreas. S. A. Bencosme. —p. 87.

Thyroid Cancer Caused by Radioactive Iodine.—In earlier investigations Goldberg and Chaikoff observed suspicious cytological changes in the thyroid parenchyma of rats killed at various intervals after they had received single injections of radioactive iodine (I^{131}). In order to evaluate the significance of these changes, a study of the late effects of ionizing radiations emitted by this isotope was undertaken. The authors had already noted the presence of thyroid neoplasms in two rats that were killed 18 months after a single injection of 400 μc of I^{131}. Although these growths resembled thyroid cancers in man, the question of their being cancerous was left open, because criteria other than the histological appearance of the tumors were lacking. The experiments presented in this paper provide conclusive evidence that radioactive iodine can induce thyroid cancer in the rat. Thyroid cancer was encountered in 7 of 25 rats from 18 months to 2 years after they had received single injections of 400 μc of I^{131}. In five of the seven animals with thyroid cancers metastatic lesions were found in one or more of the following tissues: lung, bone, adrenal gland, lymph node, and subcutaneous tissue. Evidence that thyrotropic hormone is not the causative agent of the cancers observed in these rats was indicated by the fact that similar malignancies did not develop after prolonged treatment with propylthiouracil.

American Journal of Medical Sciences, Philadelphia

222:613-732 (Dec.) 1951

Functional Restoration of Paralyzed Diaphragm Following Cross-Union of Vagus and Phrenic Nerves. J. O. Brown and V. P. Satinsky.—p. 613.
*Confusion Between Acute Myocardial Infarction and Acute Pulmonary Embolism, Clarified by Autopsy Months After Death: Important Medicolegal Problem. S. A. Levine and J. P. Vazifdar.—p. 623.
Major Surgery in Patients with Healed Myocardial Infarction. C. A. Hannigan, F. Wroblewski, W. H. Lewis Jr. and J. S. LaDue.—p. 628.
Irreversible Post-Hypoglycemic Coma. J. F. Fazekas, R. W. Alman and A. E. Parrish.—p. 640.
*Use of Quinidine in Established Auricular Fibrillation and Flutter. D. Holzman and M. G. Brown.—p. 644.
Induced Intermittent Claudication. E. C. Texter Jr., W. Redisch and J. M. Steele.—p. 653.
Electrocardiographic Changes in Poliomyelitis. Analysis of 150 Cases. M. P. Manning and P. N. G. Yu.—p. 658.
Speranskii Method of Spinal Pumping in Treatment of Arthritis. J. H. Robbins and P. H. Settlage.—p. 663.
Clinical Experience with Anticoagulent, Tromexan. M. R. Bronstein and E. Witkind.—p. 677.
Effects of Intravenous Administration of Gelatin Solution (10%): Laboratory Study on 24 Patients with Chronic Disease. R. D. Scott and J. Ryan.—p. 686.
Fallopian Tubes. F. B. Block.—p. 697.
Physiology of Adrenal Cortex in Infancy and Childhood. A. M. Bongiovanni.—p. 710.

Myocardial Infarction and Pulmonary Embolism.—Two almost identical cases are reported in which death was presumed to have occurred from coronary thrombosis. The two men, aged 37 and 45, five weeks or seven months previously had sustained a traumatic injury of the leg. Diagnosis of acute coronary thrombosis with anterior myocardial infarction had been based on electrocardiograms taken a short while before death, and a postmortem examination had not been performed. In both cases litigation developed as to whether the death was due to the accident. Differential diagnosis between acute coronary thrombosis with myocardial infarction and acute pulmonary embolism is quite difficult; changes in the electrocardiogram may be erroneously interpreted as indicative of anterior myocardial infarction, while more commonly an acute pulmonary embolism may simulate posterior myocardial infarction. The authors therefore suggested that the bodies be disinterred to seek for phlebitis and pulmonary embolism as the probable causes of death. This was found to be the case in each instance, and the widows, who probably otherwise would have lost their law suits, then obtained their just compensation. Disinterment of the body and examination of the heart and lungs even months after death may serve as a valuable and decisive means to determine the cause of death and to solve equitably a controversial medicolegal problem.

Quinidine in Established Auricular Fibrillation.—Fifty-five unselected patients with established fibrillation and two with established flutter were treated with quinidine in the attempt to restore normal sinus rhythm. On the first day of treatment 0.2

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Titles marked with an asterisk (*) are abstracted.

gm. of quinidine was given orally every 2 hours for seven doses, beginning early in the morning; the individual dose was then increased by 0.1 gm. daily until the patient received 0.5 gm. every two hours for seven doses. If restoration to normal sinus rhythm occurred at any time, the patient was placed on a maintenance dose of 0.2 gm. every 6 hours, usually for a month, following which quinidine was discontinued completely. In patients who did not regain normal rhythm the average total dose was 6.1 gm. given over a period of 3.1 days, as contrasted with 3.8 gm. for 2.4 days in those with normal sinus rhythm successfully restored. Of the 57 patients, 30 had normal rhythm successfully restored, but only 14 maintained it over an average follow-up period of 6 months. The factors that operate against successful restoration are long duration of the arrhythmias, the presence of cardiac enlargement or a history of cardiac failure, and the presence of rheumatic heart disease. Occasionally, a second attempt is successful when the first has failed. Of the 57 patients, 28 had symptoms of cinchonism, which only occasionally were severe enough to necessitate discontinuing the drug. None of the manifestations of drug idiosyncrasy, such as syncope convulsions, collapse, respiratory embarrassment, or sudden death, were observed. Significant electrocardiographic changes consisted in slowing of auricular impulse formation, with a tendency to regular ventricular response; increase in intraventricular conduction time; increase in intraauricular conduction time in patients whose normal rhythm was restored (enlargement of the P waves) and evidence of ventricular irritability.

American Journal of Obstetrics & Gynecology, St. Louis

62:1187-1416 (Dec.) 1951. Partial Index

*Physiologic Study of Acute Renal Failure, with Follow-Up Observations. L. C. Chesley and W. H. McCaw.—p. 1187.
Malignant Tumors Involving Vulva. C. G. Collins, J. H. Collins, E. W. Nelson and others.—p. 1198.
Vulval Cancer: Critical Review. W. K. Diehl, J. W. Baggett and J. H. Shell.—p. 1209.
Basal-Cell Carcinoma of Vulva: Report of Five Cases and Review of Literature. A. M. Siegler and H. J. Greene.—p. 1219.
*Labor and Delivery After Cesarean Section. A. L. Wilson.—p. 1225.
Chronic Ulcerative Colitis and Pregnancy. M. S. Kleckner Jr., J. A. Bargen and E. A. Banner.—p. 1234.
External Endometriosis. J. W. Huffman.—p. 1243.
Improved Pudendal Block Anesthesia with Hyluronidase. G. W. Douglas and L. F. Vosburgh.—p. 1253.
Perforation of Uterus. P. M. Murray and L. B. Winkelstein.—p. 1262.
Influence of Vitamin D on Vaginal Epithelium of Menopause and Postmenopause. N. Freedman.—p. 1273.
The Menopausal Syndrome: Study of Case Histories. J. C. Donovan.—p. 1281.
Use of Dilute Infusion of Pituitrin in Obstetrics. J. S. Labate and A. J. Barbaro.—p. 1292.
Efficiency of Placental Exchange in Human Subject at Time of Delivery as Determined by Radiosodium Tracer Techniques. I. H. Kaiser and I. M. Cushner.—p. 1300.
Surgically Removed Ovary. J. E. Hall.—p. 1307.
Spinal Anesthesia in Obstetrics. N. M. Bittrich and J. S. Rangatore.—p. 1314.
Effect of Conization of Cervix on Subsequent Pregnancy: Preliminary Report. P. K. Champion and N. J. Thompson.—p. 1321.
Management of Abortion at the Cook County Hospital. A. Webster. 1327.
Complete Perineotomy. E. D'Errico and R. P. McKeogh.—p. 1333.

Acute Renal Failure.—Chesley and McCaw point out that acute renal failure is of particular importance in obstetrics, because pregnancy and delivery involve complications that may produce renal failure, including severe toxemia, abruptio placentae, shock caused by hemorrhage, or septic abortion. Isoimmunization to the Rh factor also predisposes to renal failure should the patient be transfused with Rh-positive blood. The authors reviewed the laboratory records of 114 patients whose blood nonprotein nitrogen levels exceeded 60 mg. per 100 ml. Of these, 25 were accepted as having acute renal failure, the chief criterion for the diagnosis being acute and severe reduction in the concentration of urea and creatinine, together with a history of prolonged shock or some other factor known to be associated with the syndrome. Other criteria were fixation of the urinary specific gravity, presence of heme pigments in the urine, oliguria, and transient hypertension. The most frequent precipitating factor was abruptio placentae. Eight of the 25 patients died, probably none from renal failure per se. The most frequent cause of death was prolonged, irreversible shock, which had produced the renal failure in these cases. It was found that in acute renal failure, the kidney concentrates urea and uric acid only one to three times, and creatinine and potassium from two to five times. The sodium concentration in the urine approaches that in plasma because of the inability of the kidney activity to reabsorb it. The inability of the kidney to concentrate the nitrogenous wastes and potassium persists into the third week. Diuresis antedates recovery of concentrating power. The renal tubules lose the capacity for the active reabsorption of uric acid, which explains why the uric acid clearance is disproportionately high during recovery from acute failure. The tubules may excrete potassium in acute renal failure. The clearances of *p*-aminohippurate and inulin and the maximal tubular excretory capacity for *p*-aminohippurate are greatly depressed, and return to normal only over a period of months. The authors believe that glomerular filtration is impaired for weeks.

Labor and Delivery After Cesarean Section.—Wilson found that in his service about 1.5% of the pregnant women have a history of a previous cesarean section. He reviews 943 consecutive viable pregnancies following cesarean section observed from 1932 to 1950. There were 15 cases of uterine scar rupture, in 9 of which it was complete. There was no maternal mortality attributable to rupture of a cesarean scar, but there was one maternal death from hemorrhage following an elective repeated cesarean section. The transverse lower segment type of cesarean section is safest for future pregnancies. There were no infants lost due to rupture of a low transverse scar, and no complete ruptures of this type. Maternal morbidity is 7½ times greater with repeated cesarean sections than in vaginal delivery. The rise to 41% vaginal deliveries after previous cesarean section in 1950 with no maternal mortality or morbidity, no ruptures, and no fetal mortality indicate the increasing safety of this method. In 50% of the cases of scar rupture there had been fever or infection following the previous section. Palpation of the uterus abdominally or subjective tenderness are not reliable indicators of impending rupture. Of six repeated cesarean sections for "impending rupture," four showed no evidence of rupture of the scar. All seven fetal deaths occurred with complete rupture of the classic type of scar. Three of the infants were lost at rupture before the 39th week. If all patients who had had a previous cesarean section were routinely subjected to another section two weeks before term, there would still be a few spontaneous ruptures prior to this time. If the previous classic scar appears intact and sound at the second section, a low transverse incision should be made. Routine placentography is suggested because placental implantation over the scar area is presumably more conducive to rupture. The character of labor, position, size of the fetus, and pelvic structure may be deciding factors as to mode of delivery, regardless of the scar of a cesarean section.

American Journal of Surgery, New York

83:1-124 (Jan.) 1952

Branchial Cysts and Fistulas: Study of 75 Cases Relative to Clinical Aspects and Treatment. C. E. Sedgwick and J. F. Walsh.—p. 3.
Duodenal Diverticula. P. Glasier and A. J. Corbett.—p. 9.
Carcinoma of Ampulla of Vater. G. L. Beale and A. S. Trulock Jr.—p. 20.
Nephrocalcinosis. M. M. Schapiro, J. R. Duron and A. Midence.—p. 26.
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Primary Carcinoma of Fallopian Tube. M. E. K. Johnson and T. G. Amos.—p. 35.
Ovarian Pregnancy. R. E. Taber and E. S. Crossett.—p. 41.
*Fatal Pulmonary Emboli: Study of 130 Autopsy-Proven Fatal Emboli. J. J. Byrne and E. E. O'Neil.—p. 47.
Value of Parenteral Nutrition in the Poor Risk Surgical Patient. C. O. Rice, P. Bauer and J. H. Strickler.—p. 50.
Multiple Primary Malignant Tumors Involving Colon and Rectum: Report of 94 Cases. H. E. Bacon and M. C. Tavenner.—p. 55.
Complications of Abdominal Colostomy. W. Birnbaum and P. Ferrier.—p. 64.
Treatment of Massive Rectal Prolapse. C. B. Ripstein.—p. 68.

Fatal Pulmonary Emboli.—A study was made of 130 cases of autopsy-proven fatal pulmonary emboli occurring at the Boston City Hospital from 1942 through 1949. Only emboli believed to be the immediate cause of death were studied, eliminating

a large group of cases in which incidental pulmonary emboli were found. Conditions associated with development of fatal emboli were cardiac disease and postoperative states in 48 and 33 cases, respectively, hemiplegia in 22 cases, neoplasm in 11 cases, ambulatory phlebitis in 8 cases, and miscellaneous diseases in 8 cases. It is of interest that no obstetric cases are represented in the series. Each group of diseases was analyzed further, with special attention given to the source of the emboli and the presence of leg signs whenever the leg veins were the source. In 91% of the cases the emboli came from the leg veins, and the majority of these patients had signs of phlebitis of the legs. Eight of the patients had had some form of surgical interruption of the deep veins to prevent embolization. Investigation of the reasons for the failure convinced the authors that only division of the veins with removal of a segment of the vein can prevent recanalization.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

36:1-100 (Jan.) 1952

Cultivation of Treponemes with Preservation of Characteristic Morphology. N. R. Rose and H. E. Morton.—p. 1.
Morphologic Variation of Treponema. N. R. Rose and H. E. Morton. —p. 17.
Studies on Life Cycle of Spirochetes: IX. Studies in Filterable Phase of Spirochetes. M. Haanes, E. D. DeLamater and V. R. Saurino.—p. 38.
Presumptive False Positive Serologic Reactions for Syphilis in Central America: I. Incidence and Distribution. G. Stout, M. Guzmán and N. S. Scrimshaw.—p. 41.
Id.: II. Relation to Serum Ascorbic Acid, Riboflavin, Alkaline Phosphatase, Carotene, and Vitamins A and E in Blood Serum. G. Stout, M. Guzmán and N. S. Scrimshaw.—p. 49.
Id.: III. Relation to Serum Protein, Albumin, and Globulin. G. Stout, J. Méndez, M. Guzmán and N. S. Scrimshaw.—p. 55.
Id.: IV. Relation to Positive Reactions for Cephalin Cholesterol (Hanger) Flocculation Test. G. Stout, F. Aguirre and N. S. Scrimshaw.—p. 60.
Studies in Cardiovascular Syphilis: II. Methodologic Problems in Evaluation of Therapy. P. M. Densen, P. Padget, B. Webster and others. —p. 64.
*Effect of ACTH on Jarisch-Herxheimer Reaction and on Lesions of Experimental Syphilis in Rabbit. W. H. Sheldon, A. Heyman and L. D. Evans.—p. 77.
Therapeutic Paradox (?) in Cardiovascular Syphilis. C. F. Mohr and R. D. Hahn.—p. 82.
Primary Cutaneous Infection with Neisseria Gonorrheae. M. Marmell. —p. 88.
Syphilitic Interstitial Keratitis After Five Years of Seronegativity: Case Report. R. C. V. Robinson.—p. 92.

Effect of Corticotropin on Jarisch-Herxheimer Reaction.—Multiple skin syphilomas were produced on the backs of six male albino rabbits by intradermal inoculation of 0.1 ml. of a saline suspension of the Nichols strain of Treponema pallidum. A few days after the appearance of the lesions one syphiloma was excised as a control and corticotropin (ACTH) in daily doses of 5 mg. per kilogram of body weight was administered intramuscularly in three divided doses per day. On the third day of corticotropin therapy one and sometimes two of the skin lesions were excised. Immediately afterwards, three doses of 10,000 units of crystalline penicillin in aqueous solution were given intravenously at three hour intervals, while corticotropin therapy was continued for another day. The remaining syphilomas were excised at two hour intervals following the initial injection of penicillin. Results showed that the administration of corticotropin did not prevent the occurrence of the morphological manifestations of the Herxheimer reaction, which consisted of transient acute inflammatory cell infiltration in the syphilitic lesion. The changes were similar to those observed in the syphilitic lesions of human beings and animals receiving penicillin alone. In fact, the hormone caused a diminution of the inflammatory cell infiltration in the syphilitic lesions, and thus created a background against which the acute inflammatory response associated with the Herxheimer reaction became more obvious. The failure of corticotropin to alter the Herxheimer reaction does not disprove that this phenomenon is a hypersensitivity reaction, but suggests that corticotropin does not interfere with the basic mechanism of the delayed type of hypersensitivity reaction, while it may exert an inhibiting effect on the associated inflammatory response. The long-term effect of corticotropin on untreated syphilitic infection in rabbits was studied in another group of six animals infected by intradermal inoculation of T. pallidum. In addition two of these animals had been given intravenously 3 cc. of the same suspension of T. pallidum. In two of the six animals corticotropin therapy was begun on the day of the appearance of the skin lesions and was continued for 30 days, while in four animals the drug was administered 4 days prior to inoculation and was continued for 90 days. Results indicated that prolonged administration of large doses of corticotropin to rabbits with experimental syphilis did not alter the host response sufficiently to change the natural cause of infection. The hormone diminished, but did not completely suppress, the intensity of the inflammatory cell response in the syphilitic lesions, but the proliferative reparative processes in the lesions were distinctly inhibited. There was apparently no significant increase in the number of demonstrable treponemas in the lesions.

American Surgeon, Atlanta, Ga.

18:1-100 (Jan.) 1952

Use of Von Petz Clamp in Combined Abdominoperineal Resection of Rectosigmoid. J. D. German.—p. 3.
Thoracoplasty in Treatment of Pulmonary Tuberculosis. O. C. Brantigan. —p. 6.
Evaluation of Lumbar Sympathectomy. W. H. Kisner and H. Mahorner. —p. 30.
*Congenital Arteriovenous Anomalies of Cerebral Cortex, Their Surgical Treatment. H. S. Swanson.—p. 36.
*Xeroderma Pigmentosum. W. S. Brockington and R. W. Postlethwait. —p. 50.
Statistical Study of Tuberculosis of Bones and Joints in Children. S. W. Allred and W. L. Minear.——p. 58.
Stab Wounds of Heart and Pericardium Producing Acute Cardiac Tamponade: Treated by Aspiration of Pericardium; Report of Cases. C. V. Menendez.—p. 66.
Operation for Difficult Sliding Hernia of Large Bowel. A. R. Koontz. —p. 78.
Modified Technic for Total Gastrectomy with Formation of Food Pouch from Jejunum. C. J. Hunt and J. S. Cope.—p. 85.

Surgical Treatment of Congenital Arteriovenous Anomalies.—Surgical treatment of a congenital arteriovenous anomaly of the cerebral cortex is feasible when roentgenograms and angiograms indicate that it may be removed without additional incapacitating neurologic disabilities. On the other hand, coagulation or ligation of the superficial vessels may increase the size and mass of the arterial anomaly and increases the possibility of hemorrhage. Extracranial ligation of the carotid artery is not advisable, since collateral circulation lessens the normal circulation to the remaining areas of the brain. Once the intervention is justified, the main technical difficulty during removal is to control potentially massive hemorrhage without injuring the adjacent uninvolved cortex. If this appears impossible, the operation should be discontinued. Exploration of the cortex with needles is contraindicated. Careful and complete control of the arterial supply is best begun proximally, and in most instances it is obtained with silver clips or silk ligatures doubly tied. Low voltage cauterization may be sufficient for small arteries. After a complete superficial arterial denudation, a cortical incision is made and each incoming artery branch is controlled. When hemorrhage from the draining veins ensues, and its control is almost impossible because identification of the bleeding vessels is very difficult, the only recourse is quick enucleation of the mass with prompt control of the deep arterial supply. The mass is rolled distally in the direction of the draining veins. Bleeding that occurs at this stage is controlled by direct pressure, and the draining veins are ligated. If thrombosis occurs postoperatively, anticoagulation therapy may be effective. After six or eight weeks comparative angiograms should be carried out routinely. During one intervention Gardner's method of exsanguination was attempted without assistance in diminishing hemorrhage. In another intervention for a very large arteriovenous aneurysm the author resorted to total spinal anesthesia in an attempt to minimize the technical problem. Scalp hemostasis or control of dural oozing was not needed, total removal of the large mass was effected with extreme ease, and less than one pint of blood was lost. It is suggested that total spinal anesthesia may become a good adjuvant in other surgical interventions in which an adequate control of hemorrhage is necessary.

Xeroderma Pigmentosum. — Xeroderma pigmentosum is reported in 13 members of five generations of a family. No medical description or death certificate is available for the cases that occurred prior to 1920, but reliable information was given by the grandmother of a 5-year-old child who died in 1948. She had observed all these cases except the first and the second, but was told that these two, her uncle and aunt, had died of the same disease at the ages of 5 and 3. The last five patients have died since 1941. Hyperkeratosic areas, photophobia, conjunctivitis, ectropion, or blindness justified the diagnosis of xeroderma pigmentosum with malignant degeneration. There was evidence that the disease had been transmitted by simple recessive genes rather than by sex linkage. No treatment was effective. Excision, sometimes followed by full-thickness grafts, was palliative, but malignant ulceration developed in other areas. Podophyllotoxin controlled some areas of carcinoma temporarily. Treatment with x-rays is contraindicated in that severe reactions occur in the surrounding skin and new lesions appear. As soon as the disease is recognized, exposure of the skin to light must be prevented. *p*-Aminobenzoic acid may be used as a protective ointment; large intake of vitamins seems to be of some value.

Angiology, Baltimore

2:425-604 (Dec.) 1951

Rational Priciples in Treatment of Spontaneous Arterial Occlusions. R. Leriche.—p. 430.
*Chronic Edema of Lower Limbs. F. Martorelli.—p. 434.
Phenomenon of Stress in Relation to Human Essential Hypertension. G. de Takats.—p. 461.
Present Status of Treatment of Frostbite. H. B. Shumaker Jr.—p. 476.
*Intrasaccular Wiring of Abdominalarteriosclerotic Aortic Aneurysm by "Pack" Method. R. R. Linton.—p. 485.
Present Status of Arteriography of Peripheral Vessels. F. B. Wagner Jr. —p. 499.
Recent Advances in Surgery for Obliterative Arterial Disease. G. H. Pratt.—p. 517.
Clinical Applications of Adrenergic Blockade in Vascular Diseases with Special Reference to Dibenamine and 688A. H. Haimovici.—p. 531.
The Heart in Generalised Scleroderma: Progressive Systemic Sclerosis. R. H. Goetz.—p. 555.
Vein Inlay Graft in Treatment of Aneurysms and Thrombosis of Abdominal Aorta: Preliminary Communication with Report of 3 Cases. N. E. Freeman and F. H. Leeds.—p. 579.
Tryptar in Treatment of Diabetic Gangrene. S. S. Samuels.—p. 589.

Chronic Edema of Lower Limbs.—The prolonged accumulation of interstitial plasma in the tissues is known as chronic edema. Chronic edema of the extremities has two fundamental causes: disturbance of the venous circulation or venous edema (phlebedema), or disturbance of the lymphatic circulation (lymphedema). Venous edema is distal, depressible, and easily reducible by recumbency. It often causes dermatitis, pigmentation, and ulcers. It occurs as a result of deep valvular insufficiency, essential or postphlebitic, or as a result of venous obliteration, but rarely from the presence of a congenital or acquired arteriovenous fistula. The treatment of valvular insufficiency by deep ligation usually increases the edema. Lymphedema differs from venous edema by being less common, harder, scarcely depressible, less reducible by recumbency, and total or rhizomelic in localization. It may be divided into congenital, essential, and secondary. In essential lymphedema the treatments indicated are lymphangioplastic surgery and cutaneous plastic surgery. Venous edema and lymphedema favor streptococcic infections. These provoke fibrous hyperplasia of the skin, the subcutaneous cellular tissue, and aponeurosis, and finally the edema becomes irreversible and totally irreducible by recumbency, in a form partly corresponding to the so-called elephantiasis and called fibroedema by the authors. Finally, the author mentions erythrocyanoid lipedema, an orthostatic edema with adiposity of the legs forming a supramalleolar ischemia with coldness, cyanosis, and ultimately ulcers, which can be relieved by lumbar sympathectomy.

Intrasaccular Wiring of Aortic Aneurysms.—This report is based on 27 patients with the arteriosclerotic type of aneurysm. Linton briefly cites various therapeutic methods that have been tried, pointing out that ligation of the aorta has given disappointing results. Resection of the aneurysm with the insertion of a blood vessel graft or a plastic prosthesis may prove more efficacious, provided the patient is seen early. Another method of treatment consists of increasing the strength of the aneurysmal sac by laying on its surface sheets of cellophane or a dermal skin graft. It is, however, impossible to encircle the aneurysmal sac posteriorly, the area where rupture most frequently occurs. The "pack" method of intrasaccular wiring that was used in 22 of Linton's cases is based on the fact that the blood flow is most rapid in the main axis and slowest in the periphery of the aneurysm. It is believed that, if sufficient wire can be inserted into the sac, a thrombus will form in the periphery, thereby strengthening the wall and at the same time reducing the lumen to approximately the size of the normal aorta. The rate of blood flow in the axis of the aneurysm is sufficiently fast to prevent deposition of a clot on the numerous strands of wire that cross it, so there is little danger of complete thrombosis. Thrombosis did occur in one patient and resulted in death. The author uses the wiring trocar of Blakemore, and a stainless steel alloy wire, 0.010 in. in diameter. The first few feet of wire are passed manually. The wiring cannot be completed through the initial puncture site. The trocar is reinserted in several places and directed toward the areas that still show expansile pulsation. The smallest amount of wire inserted was 100 ft. (31 m.) and the greatest 960 ft. (295 m.). The mean for all the cases was 307 ft. (95 m.). An abdominal aneurysm can be wired most effectively by a transabdominal exposure under a general anesthesia. Seventeen patients survived the wiring, but three of them died before six months had elapsed and these cases are regarded as failures. At least 15 of the 17 who survived the procedure were benefited at least temporarily.

Annals of Internal Medicine, Lancaster, Pa.

35:1175-1444 (Dec.) 1951

*Terramycin Therapy of Pneumonia: Clinical and Bacteriologic Studies in 91 Cases. G. G. Jackson, T. H. Haight, E. H. Kass and others. —p. 1175.
Current Concepts of Beryllium Poisoning. H. S. Van Ordstrand.—p. 1203.
Management of Lung Abscess, with Special Reference to Place of Antibiotics in Therapy. E. H. Drake and F. M. Sones Jr.—p. 1218.
*Study of Use of Radioactive Gallium in Medicine. F. R. Lang.—p. 1237.
*Quantitative Evaluation of Contribution of Nitrogen Mustard to Therapeutic Management of Hodgkin's Disease. A. Gellhorn and V. P. Collins.—p. 1250.
Extrathyroidal Hypermetabolism: Classification and Discussion Including Three Illustrative Case Reports. M. Bruger and V. P. Hollander. —p. 1260.
Disturbances of Cardiac Rhythm and Conduction in Congenital Cardiac Disease: Report of 5 Cases. H. M. Rogers.—p. 1276.
Psyche and Soma: Spiritual and Physical Attributes of Heart. P. D. White.—p. 1291.
Mechanism of Gallop Sounds, Studied with Aid of Electrokymograph. P. T. Kuo, E. A. Hildreth and C. F. Kay.—p. 1306.
Further Observations on Use of Liberalized Diets in Treatment of Diabetes. H. J. John.—p. 1318.
Variability of Signs in Multiple Sclerosis. I. C. Sherman.—p. 1329.
Myocardial Involvement in Acute Nonspecific Pericarditis: Report of Three Cases. J. Godfrey.—p. 1336.

Terramycin Therapy of Pneumonia.—Of 91 patients with pneumonia treated with terramycin, 68 had pneumococcal pneumonia, 6 had clinical and roentgen-ray findings consistent with the diagnosis of pneumococcal lobar pneumococci but laboratory examination was negative for pneumococci, 4 had primary atypical pneumonia, and 13 had nonpneumococcal bacterial pneumonia. The most frequent dosage regimen employed was 0.5 gm. of terramycin orally every four hours, a single starting dose of 1 gm. being used in about two-thirds of the pneumococcal cases and in about one-half of the other cases. Some patients required an increase of the interval between doses from four to six hours because of failure to tolerate the drug. In the great majority of the patients the total oral dose was between 10 and 30 gm. given over a period of from 4 to 10 days. Treatment was given intravenously in only four patients. The bacteriological results and the immediate clinical effects indicated that terramycin was highly effective against pneumococcal pneumonia. In most of the other pneumonias in which a bacterial etiology was proved or suspected and in the four cases of primary atypical pneumonia, the immediate effects of terramycin therapy were also favorable. Replacement of the flora of the sputum by staphylococci, slow clearing of the lungs, and recurrence or

persistence of leukocystosis indicated that the beneficial effects of terramycin were, in part, vitiated in many of the authors' patients by superinfections with pathogenic strains of Staphylococcus aureus. Gastrointestinal symptoms from terramycin were frequent and in many patients were quite severe, adding considerably to the morbidity of many who recovered. In many of the patients with terramycin-induced diarrhea, the fecal flora was replaced by pathogenic staphylococci. In five of seven patients who died the toxic effects of terramycin on the gastrointestinal tract may have contributed in large measure to the fatal outcome. In addition, staphylococci were important pathogenetically in the lungs of four patients.

Use of Radioactive Gallium in Medicine.—Gallium is a rare metal with a low melting point (30 C) and a boiling point of 1,700 C. Gallium has several isotopes. Because of the short half-life (14.3 hours) and its gamma irradiation of 2.53 mev and beta irradiation of 2.50 mev, Ga^{72} was selected as the ideal isotope of this metal for human application. Toxicity studies in animals showed that the dosage levels required for radioactive gallium in man are well below the danger zone. The established tracer dose for diagnostic use is 350 to 400 μc. The authors studied six patients with carcinoma of the prostate, two with carcinoma of the breast, and one each with bronchogenic carcinoma, gastric carcinoma, osteogenic sarcoma and osteochondrosarcoma. All had bone metastases. In each instance after administration of radioactive gallium, Geiger-Müller counts taken over every metastatic lesion demonstrated by x-ray survey of the bones showed a 20-fold increase above those of normal bone in the adjacent areas. On several occasions, areas of bone were observed that emitted increased irradiation after the administration of radioactive gallium and in which no x-ray evidence of metastases could be found. Undoubtedly these were bone areas in which metastases were forming at a stage too early to be demonstrated by roentgenograms. Only two attempts have been made thus far to use Ga^{72} therapeutically in patients with malignant bone lesions. It is still too early to evaluate the ultimate effect of radioctive gallium on such patients, but information thus far obtained in these two cases strongly indicates that this isotope at least has a palliative effect in prolonging life and in relieving bone pain and other distressing symptoms. The short-life of Ga^{72} makes control of the radiation dosage much easier and reduces the possibility of prolonged harmful residual radiation effects. Because of its selective location in the bony structures of the body, these therapeutic advantages over other materials warrant further investigation.

Nitrogen Mustard in Management of Hodgkin's Disease.—The course of Hodgkin's disease in 67 patients who received irradiation and nitrogen mustard in alternate courses has been compared with that in 65 patients who received radiotherapy alone. For the majority of the patients 0.2 mg. of methyl bis (beta chloroethyl) amine per kilogram of body weight on two successive days was the most satisfactory nitrogen mustard regimen. The four-year survival rate from the onset of symptoms, from the time of definite diagnosis by biopsy, or from the time of evident generalized disease was not significantly different in the two groups of patients. It has been concluded, therefore, that the addition of nitrogen mustard to the therapeutic regimen of irradiation does not modify the duration of life expectancy of the disease. It was demonstrated, however, that the amount of time necessary for irradiation treatments was reduced by one-half in the patients receiving irradiation and nitrogen mustard as compared with patients receiving radiotherapy alone, suggesting that the amount of irradiation required is less, the asymptomatic period greater, and economic burden lighter for the patients on the former therapeutic regimen than on the latter. The incidence of serious toxicity in the 144 courses of nitrogen mustard given to the 67 patients was 7%. One death occurred in a patient due to a miliary dissemination of pulmonary tuberculosis following the administration of nitrogen mustard. Immediate subjective and objective improvement followed 78% of the courses of nitrogen mustard. It is concluded that nitrogen mustard is a useful adjuvant to radiotherapy in the management of Hodgkin's disease, although it does not prolong life.

Antibiotics & Chemotherapy, Washington, D. C.

1:545-600 (Dec.) 1951. **Partial Index**

Study of Effects of Procaine Penicillin G in Gelled Oil Following Intravenous Administration. S. W. Handford and N. V. Ricchiuti.—p. 545.
Study on Efficacy of Viomycin, Chloramphenicol and Polymyxin B on Pasteurella Multocida. G. A. Gorzynski and E. Neter.—p. 554.
Chemotherapeutic Trails Against Experimental Rat Arthritis. K. A. Ludwig and F. J. Murray.—p. 557.
In Vitro Comparative Study of Inhibitory Activity of Certain Antibiotics in Low and High Concentrations. C. W. Johnson and T. W. Johnson.—p. 560.
Actinomycin from Species of Genus Micromonospora. W. P. Fisher, J. Charney and W. A. Bolhofer.—p. 571.
*Treatment of Enterobiasis with Terramycin Base. E. H. Loughlin, I. Rappaport, W. G. Mullin and others.—p. 588.
Nigericin, New Crystalline Antibiotic from Unidentified Streptomyces. R. L. Harned, P. H. Hildy, C. J. Corum and K. L. Jones.—p. 594.

Terramycin Base for Enterobiasis.—Observations by Wells on the effiicacy of terramycin hydrochloride on pinworms in mice and in human subjects prompted Loughlin and associates to try the intermediate amphoteric form of terramycin, known as terramycin base, in the treatment of enterobiasis. Since they were studying terramycin base as a therapeutic agent in yaws, and since a number of patients with yaws also were infected with pinworms, it was simple to evaluate the efficacy of terramycin base in the latter infection in 30 patients. The diagnosis of enterobiasis was established by examining Scotch tape impressions of the anal and perianal skin folds for the presence of the eggs of Enterobius vermicularis. In view of the fact that the cycle of maturation of Enterobius from egg to egg requires from 15 to 28 days, and since no adequate measures to prevent these patients from becoming reinfected could be provided, the authors believed that a period of 35 days of observation after completion of treatment would be sufficient for determining the possibility of relapse. Terramycin base was administered in single, daily doses graded according to age of the patients as follows: to patients less than 5 years of age, 1 gm.; to patients between 5 and 10 years, 1.5 gm.; to patients over 10 years, including adults, 2 gm. Although the authors usually gave these doses for five days, they now believe that treatment should be continued for seven days. They feel that terramycin base has provided better results in the treatment of patients infected with pinworms than has any other anthelminthic. Advantages are lack of toxicity and the fact that supplementary measures such as cathartics, colon irrigations, and restricted diets are unnecessary.

Blood, New York

7:1-96 (Jan.) 1952

Studies on Radiosensitivity of Bone Marrow: Relative Sensitivity of Erythroid and Myeloid Elements. W. N. Valentine and M. L. Pearce.—p. 1.
Id.: II. Effect of Large, Repeated Whole Body Irradiation Exposure on Hematopoiesis. W. N. Valentine, M. L. Pearce and J. S. Lawrence.—p. 14.
Hemorrhagic Diathesis Due to Circulating Anticoagulant: Report of Case with Laboratory Observations. E. R. Pons Jr. and M. V. de Torregrosa.—p. 20.
Infectious Mononucleosis: Prognostic Significance of Various Changes of Blood Leukocytes. J. E. Stevens, E. D. Bayrd and F. J. Heck.—p. 31.
Multiple Spontaneous Remissions in a Child with Acute Leukemia: Occurrence of Agranulocytosis and Aplastic Anemia in Acute Leukemia and Their Relationship to Remissions. F. A. Bassen and J. L. Kohn.—p. 37.
Studies on Abnormal Hemoglobins: III. Interrelationship of Type S (Sickle Cell) Hemoglobin and Type F (Alkali Resistant) Hemoglobin in Sickle Cell Anemia. K. Singer and A. I. Chernoff.—p. 47.
*Studies on Platelets: II. Effect of Transfusion of Platelet-Rich Polycythemic Blood on Platelets and Hemostatic Function in "Idiopathic" and "Secondary" Thrombocytopenic Purpura. M. Stefanini, J. B. Chatterjea, W. Dameshek and others.—p. 53.
Interrelationships of Factors That Influence Megaloblastic Anemias. R. H. Girdwood.—p. 77.

7:97-190 (Supplement to Jan.) 1952

Proceedings of the Second Conference on Folic Acid Antagonists in Treatment of Leukemia. S. Warren and others.—p. 97.

Transfusion of Platelet-Rich Blood in Thrombocytopenic Purpura.—Platelet-rich polycythemic blood, by the multiple syringe technique and siliconized apparatus, was transfused by Stefanini and associates in 14 cases of idiopathic ("megakaryocytic") and 8 of secondary ("amegakaryocytic") thrombocytopenia in order to study the effects on platelet number and function and on

hemorrhagic manifestations. Platelets disappeared rapidly from the circulation (in from ½ to 12 hours) and in the 12 patients with acute idiopathic thrombocytopenia and in 1 patient with chronic thrombocytopenia with a low platelet count. They disappeared more slowly (24 hours) in the other case of chronic idiopathic thrombocytopenia in which there was a higher platelet count. Essentially similar platelet disappearance curves were obtained in two patients before and after unsuccessful splenectomy. In the patients with secondary thrombocytopenia, the survival of platelets in the circulation was much longer (average 48 to 96 hours). Behavior of clot retraction and prothrombin activity of serum paralleled closely that of the platelet count. The bleeding time and capillary fragility usually remained improved for 24 to 48 hours after the platelet count had fallen to the initial level, and the hemorrhagic manifestations also were improved in every case for many hours. Similar but less marked beneficial effects on the hemorrhagic manifestations were obtained with transfusions of blood from donors with normal platelet counts, provided fresh blood was used and precautions taken to prevent excessive loss of platelets. Remissions were observed in two patients with idiopathic thrombocytopenia following direct transfusion of polycythemic blood. In both cases the injected platelets disappeared promptly from the circulation but within 24 hours the platelet count began to rise and a long-sustained remission followed. This suggests that polycythemic blood may contain a stimulatory principle that can induce or accelerate a spontaneous remission. The authors conclude that the prompt disappearance of injected platelets from the circulation of patients with idiopathic thrombocytopenia suggests the presence of a humoral destructive mechanism that is not present in the secondary or amegakaryocytic cases. This destructive factor does not appear to originate in the spleen. These observations do not exclude the existence of an inhibitory effect upon platelet production from the megakaryocytes of the bone marrow. Polycythemic blood may contain a platelet stimulatory factor.

California Medicine, San Francisco

76:1-54 (Jan.) 1952

Modern Use of Urinary Antiseptics. F. Hinman Jr.—p. 1.
Medical Aspects of Civil Defense in California. J. J. Stein.—p. 8.
Fractures About Elbow in Children. F. J. Cox, M. T. Hurley and R. B. Compton.—p. 13.
*Needle Biopsy of Liver: General Considerations. W. E. Mollie and L. Kaplan.—p. 16.
Prolonged Labor. P. H. Arnot.—p. 20.
Psychosomatic Problems in Urology. A. Auerback and D. R. Smith.—p. 23.
Malignant Tumors of Childhood. R. E. Knutti.—p. 27.
Evaluation of New Method of Dust Control. M. C. Harris and N. Shure.—p. 30.
Problem of the Mentally Defective Child. P. Cohen.—p. 34.
Infraclavicular Chest Wall Tumors in Hodgkin's Disease. R. Goldman.—p. 38.

Needle Biopsy of Liver.—This report reviews 401 needle biopsies of the liver in 312 patients. Needle biopsy provides information about the liver that cannot be obtained readily with any other method. The chief reasons for its use are to determine the cause of liver enlargement, to establish the cause of jaundice, to distinguish between malignant disease and cirrhosis of the liver, to determine when hepatitis has subsided, and to evaluate the results of treatment. At times systemic disease that has not been recognized by other means may be diagnosed by this technique. When the biopsy diagnosis could be compared with observations at operation or autopsy, it was found that the correct diagnosis was made by biopsy in 85% of cases. Repeated biopsies provided a greater degree of accuracy. In several cases information obtained by biopsy proved that surgical treatment was unnecessary; in others the advisability of such treatment could be corroborated. The following are contraindications to needle biopsy of the liver: an uncooperative patient, impairment of the blood clotting mechanism, recent infection in the region of the biopsy, ascites (which should be removed prior to biopsy); abdominal distention, chronic passive congestion of the liver, a small liver, and complete obstructive jaundice. Needle biopsy of the liver is not without risk; the authors observed one case of fatal hemorrhage and one case of bile peritonitis; 25% of the patients had pain that radiated to the shoulder, 30% had epigastric discomfort, and 2% had pneumothorax. Other reactions and complications that might be expected but were not observed in the cases reviewed here include apprehension, friction rub, pleural hemorrhage, perforation of hollow viscus, perforation of gallbladder, atelectasis, and reaction to local anesthesia.

Cancer Research, Chicago

12:1-76 (Jan.) 1952. Partial Index

Action of Tumors on Normal Tissue Synchronously Transplanted into Anterior Chamber of Mouse Eye. H. Browning.—p. 13.
Experimentally Produced Granulosa-Cell Tumors in Rats. B. M. Peckham and R. R. Greene.—p. 25.
Identification of Aromatic Polycyclic Hydrocarbons in Carbon Blacks. H. L. Falk and P. E. Steiner.—p. 30.
Metabolism of Neoplastic Tissue: II. Survey of Enzymes of Citric Acid Cycle in Transplanted Tumors. C. E. Wenner, M. A. Spirtes and S. Weinhouse.—p. 44.
Synergistic Action of Mixtures of Certain Hepatic Carcinogens. J. C. MacDonald, E. C. Miller, J. A. Miller and H. P. Rusch.—p. 50.
Effect of Pituitary Growth Hormone (Somatotrophin) on Body Weight and Tumor Growth in C3H Mice Bearing Transplantable Mammary Adenocarcinoma. M. C. Smith, P. A. Slattery, M. B. Shimkin and others.—p. 59.
Effect of Neoplastic Tissue on Turnover of Liver Nucleic Acids. A. H. Payne, L. S. Kelly and M. R. White.—p. 65.
Marcomolecular Particles Obtained from Human Neoplastic and Non-Neoplastic Lymph Nodes: II. Electron Microscope Study. M. S. Hoster, Q. Van Winkle, J. G. Rabatin and H. A. Hoster.—p. 69.

Eye, Ear, Nose & Throat Monthly, Chicago

31:1-56 (Jan.) 1952

*Antimicrobial Therapy of Laryngeal Tuberculosis. L. J. Wallner.—p. 25.
Postoperative Cataract Lens. O. R. Wolfe, R. M. Wolfe and H. L. Wolfe.—p. 30.
*Otitis Externa, and Its Treatment with New Antibiotic Preparation. J. W. Graves.—p. 32.
Sequelae of Septal Surgery. C. B. Sputh Jr. and C. B. Sputh Sr.—p. 34.
Local Injection of Procaine Penicillin Solution in Secondary Mastoiditis. S. L. Ruskin.—p. 36.

Antimicrobial Therapy in Laryngeal Tuberculosis.—The larynx becomes involved secondary to pulmonary disease. The appearance of laryngeal lesions usually indicates a breakdown in the patients' general resistance to tuberculosis. Therefore, the treatment of the chest disease is always of primary importance. In laryngeal tuberculosis the relief of pain and hoarseness improves the morale. Improvement occurred in from 80 to 90% of patients given streptomycin for tuberculosis of the larynx. Occassionally there is complete resolution of all gross pathological changes so that the larynx appears entirely normal; more commonly, the ulceration healed and edema and infiltration subsided, but some thickening and hyperemia remained. *p*-Aminosalicylic acid can be given with good effect to patients who are resistant to streptomycin. At present, the consensus seems to be that the two drugs should be administered together, so that resistance to streptomycin is delayed, allowing prolonged therapy. Thiosemicarbazone has been used in only a small number of patients; its results have been disappointing when compared to those of streptomycin or *p*-aminosalicylic acid.

Antibiotics in Otitis Externa.—Infection of the external auditory canal has been referred to in the past as otomycosis (otitis externa mycotica), but the correctness of this terminology is questionable in the light of numerous studies of the flora in such infections. Graves cites reports from the literature that indicate that Pseudomonas aeruginosa is the organism most frequently found in external otitis and that fungi play a minor role. Staphlococcus albus is the organism most frequently found in normal ears. Acute or chronic otitis externa is accompanied by dermatitis, crusts, scales, and fissures at the meatus, and in many cases involves the tympanic membrane, thereby reducing hearing acuity. Occasionally, there is an eczematoid condition. The auditory canal has a moist coating of debris. The itching is severe and annoying; occasional bleeding from the ulcerated areas of skin generally causes the patient to consult a physician. A watery discharge resulting from the infection is also common. Graves found a preparation containing 8,000 units of polymyxin and 400 units of bacitracin per gram highly effective in 100 consecutive cases of infections of the external ear.

Florida Medical Association Journal, Jacksonville

38:455-518 (Jan.) 1952

Role of Cancer Cytology in Medical Practice. J. E. Ayre.—p. 471.
Esophageal Hiatal Hernia Associated with Myocardial Infarction. W. Stamps.—p. 472.
Absorbable Postplaced Sutures in Cataract Surgery. J. W. Taylor Jr. —p. 479.
Stress and General Adaptation Syndrome of Theories and Concepts of Hans Selye. J. G. Seltzer.—p. 481.
Aerobiologic Survey of Miami Beach District, Report of Pollen Counts for 1948 and 1949 Including Mold Spore Counts for 1949. L. Palay. —p. 485.
Changes in Compensation Law. H. G. Cole.—p. 488.

Georgia Medical Association Journal, Atlanta

41:1-36 (Jan.) 1952

Surgery in the Older Patient. H. H. Bradshaw.—p. 4.
Vocational Rehabilitation of Cardiac Patients. J. C. Massee.—p. 7.
Surgery in Treatment of Cancer of Maxillary Antrum. S. A. Wilkins Jr. —p. 9.
Sporotrichosis in Georgia. W. L. Dobes.—p. 14.
Eosinophilic Granuloma of Rib. S. B. Carter.—p. 17.

Journal of Bacteriology, Baltimore

63:1-150 (Jan.) 1952. **Partial Index**

Growth Inhibition of Tubercle Bacilli by Analogues of Biotin. H. Pope. —p. 39.
Further Observations on Persistence of Individual Strains of Escherichia Coli in Intestinal Tract of Man. H. J. Sears and I. Brownlee.—p. 47.
Resistance to Ultraviolet Light as Index to Reproduction of Bacteriophage. S. Benzer.—p. 59.
Growth of Coxiella Burnetii in Embryonated Eggs. R. A. Ormsbee. —p. 73.
Properties of Cell-Free Hydrogenases of Escherichia Coli and Rhodospirillum Rubrum. H. Gest.—p. 111.
Toxicity of Elemental Sulfur for Brucellae. V. T. Schuhardt, L. J. Rode, G. Ogelsby and C. E. Lankford.—p. 123.

Journal of Nervous and Mental Disease, New York

114:471-564 (Dec.) 1951

Glutamic Acid and Mental Deficiency. K. Albert, P. Hoch and H. Waelsch.—p. 471.
Preoperative and Postoperative Personality Changes Accompanying Frontal Lobe Meningioma. R. L. Kahn and B. Schlesinger.—p. 492.
*Neurosurgical Observations in the Multiple Sclerosis Syndrome. S. J. Rosner.—p. 511.
Deficiency State Cerebellar Syndrome. A. R. Furmanski.—p. 519.
The One and the Many. A. N. Foxe.—p. 528.
Autonomic Function in Insulin Coma Therapy. J. T. Shurley and H. M. Morris, Jr.—p. 532.

Neurosurgical Observations in the Multiple Sclerosis Syndrome.—Rosner reports on a series of patients with symptoms of multiple sclerosis who at exploratory operation had lesions differing from those found at autopsy in multiple sclerosis. The first patient had the symptoms of multiple sclerosis with amblyopia in the left eye, tremor of the intention type, ataxic gait, and slight scanning speech but no nystagmus. The significant factor suggesting some disease other than multiple sclerosis was that weakness and paresthesia were severer on the left side. Myelography disclosed a defect in the column of dye at the upper border of C5 on the right. At laminectomy, an adhesive arachnoiditis was demonstrated at C4-C5 on the right. The spinal cord in this area appeared anemic. There were no signs of plaque formation or thrombosis. The patient improved and is now gainfully employed. There has been no recurrence of the earlier symptoms during the five years that have elapsed since operation. The author presents the histories of eight other patients with symptoms suggesting multiple sclerosis in whom laminectomy was done on the basis of myelographic findings and revealed either adhesive arachnoiditis or tumors or a cyst exerting pressure on the cord. He feels that the history of symptoms being first confined to one side of the body should make one suspicious, because the multiple sclerosis syndrome may be simulated by any compressing or constricting cervical or thoracic cord lesion and these lesions are at least as numerous as the degenerative condition called multiple sclerosis. It is also his opinion that adhesive arachnoiditis is a far commoner cause of cord compression than is suspected. These adhesions may be local, that is, constricting one or two segments of the spinal cord.

Journal of Pediatrics, St. Louis

40:1-142 (Jan.) 1952

*Ferrous Sulfate Poisoning: Report of Three Cases. T. L. Duffy and A. M. Diehl.—p. 1.
Ferrous Sulfate Poisoning: Report of Fatal Case. S. C. Swift, V. Cefalu and E. B. Rubell.—p. 6.
Lipoproteins of Serum in Infancy and Childhood: I. Lipoproteins in Normal Children. C. H. Kempe, H. K. Silver, F. S. Smyth and others. —p. 11.
Id.: II. Lipoprotein Levels in Juvenile Diabetes Mellitus. J. H. Carr, C. H. Kempe, H. K. Silver and others.—p. 19.
Aplastic Anemia in Siblings with Multiple Congenital Anomalies (Fanconi Type). W. Levy.—p. 24.
Pulmonary Hypertension in Children Due to Congenital Heart Disease. F. H. Adams.—p. 42.
*Right Heart Catheterization in Patent Ductus Arteriosus and Aortic-Pulmonary Septal Defect. F. H. Adams, A. Diehl, J. Jorgens and L. G. Veasy.—p. 49.
Congenital Cirrhosis of Liver Associated with Infectious Hepatitis of Pregnancy. L. B. Bellin and I. W. Bailit.—p. 60.
Early Clamping of Umbilical Cord During Cesarean Section. S. S. Stevenson and L. H. Erhard.—p. 64.
Acute Poliomyelitis: Differential Diagnosis of 409 Revised Diagnoses. K. E. Dawson, A. C. LaBoccetta, A. S. Tornay and A. Silverstein. —p. 71.
Aureomycin in Treatment of Beta Hemolytic Streptococcal Infections. B. B. Breese.—p. 85.
Stability of Ascorbic Acid in Milk at Different Stages of Processing. A. D. Holmes.—p. 91.
Laurence-Moon-Biedl Syndrome. I. Kessel.—p. 96.
Poliosis: Report of Case in 10-Year-Old Boy. R. L. Gilman and H .H. Perlman.—p. 101.
Potassium Bromide Poisoning. R. C. Knappenberger.—p. 105

Ferrous Sulfate Poisoning.—Ferrous sulfate intoxication was observed in three infants, aged 15 months, 18 months and 26 months, respectively, who had ingested between 15 and 40 enteric, chocolate coated 5 gr. (0.3 gm.) ferrous sulfate tablets two to six hours previously. The cardinal symptoms and signs of acute ferrous sulfate poisoning were well exemplified in these three patients as follows: vomiting with retching, clear watery stools later becoming tarry, profound shocklike picture and collapse, with rapid, weak or imperceptible pulse and low blood pressure, hypotonia, hyporeflexia, dilated pupils, and the semicomatose or comatose state. Two of the patients, who had ingested between 15 and 20 tablets, recovered, while the one who according to estimation had ingested 30 to 40 tablets died. The authors emphasize that ferrous sulfate intoxication is a reality; immediate treatment of the peripheral vascular collapse with plasma and/or whole blood is imperative.

Right Heart Catheterization in Patent Ductus Arteriosus.—Of 24 patients between the ages of 1½ and 18 on whom right heart catheterization studies were performed, 8 had typical patent ductus arteriosus, 11 had atypical patent ductus arteriosus, and 5 had an aortic pulmonary defect. Results showed that right heart catheterization is of questionable value in patients with typical findings of patent ductus arteriosus on physical, roentgen, and electrocardiographic examination. On the contrary, this technique proved to be of definite value in the atypical cases. In several patients thought to have some other defect because they had only a systolic murmur audible over the left precordium or had atypical diastolic murmurs, abnormal function as shown on electrocardiograms, with right axis deviation, and roentgen findings not consistent with typical patent ductus arteriosus, cardia catheterization clearly demonstrated a patent ductus arteriosus. These patients thus received the benefit of surgical ligation. In several instances the diagnosis was proved before surgery by passing the catheter through the ductus arteriosus and down into the aorta. Although some patients had large shunts with normal pulmonary artery pressures, most of the patients with elevated pressures had large shunts. Increasing cardiac disability seemed to be related more to the increase in pulmonary artery pressure than to the size of the shunt. Data on five patients with aortic-pulmonary septal defects showed that in some instances it is possible to pass the catheter through the defect into the aorta, thus proving the diagnosis. This can be distinguished from the situation where the catheter has passed through the ductus arteriosus into the aorta by the anterior position of the catheter in the lateral view. One paient died during the surgical attempt to close the septal defect, and at postmortem examination the diagnosis was confirmed. This is the first instance of such a diagnosis being made before death and confirmed at necropsy reported thus far in the literature.

Journal of Thoracic Surgery, St. Louis

23:1-110 (Jan.) 1952

Constrictive Pericarditis and Constrictive Pleuritis Treated by Pericardiectomy and Pulmonary Decortication: Report of Case. R. H. Overholt, C. S. Burwell, J. W. Woodbury and J. H. Walker.—p. 1.
*Direct Intracardiac Relief of Pulmonary Stenosis in Tetralogy of Fallot. R. P. Glover, C. P. Bailey, T. J. E. O'Neill and others.—p. 14.
*Treatment of Coronary Artery Insufficiency by Implantation of Internal Mammary Artery into Left Ventricular Myocardium. A. Vineberg.—p. 42.
Congenital Cystic Disease of Lung Associated with Anomalous Arteries. F. G. Kergin.—p. 55.
Physiology and Cytology of Pulmonary Edema and Pleural Effusion Produced in Rats by Alpha-Naphthyl Thiourea (ANTU). C. P. Richter.—p. 66.
Late Results in Treatment of Pulmonary Tuberculosis by Thoracoplasty: Review of Two Series. G. C. Adie, W. G. Childress, H. J. Brezing and D. Taylor.—p. 92.
Surgical Significance of Calcified Parabronchial and Paratracheal Lymph Glands. E. R. Maurer.—p. 97.

Intracardiac Relief of Pulmonary Stenosis.—The direct intracardiac relief of pulmonary stenosis has been attempted in 30 consecutive patients with the tetralogy of Fallot between the ages of 2 months and 36 years. In 15 of these patients there was stenosis of the pulmonary valve, in 12 an obstructing malformation of the pulmonary conus area (infundibulum), and in the remaining three a localized constriction in the main pulmonary artery distal to a normal pulmonary valve but proximal to the bifurcation of this vessel into its right and left major branches. The technique for the relief of valvular stenosis consisted of dividing the stenosed valvular cone with a Brock type valvulotome into a bicuspid valve and then passing the left index finger, or largest urethral sound, through the divided valve to insure patency without further rupture of the valve or vessel. For the relief of a high infundibular obstruction the proper sized flat-handled valvulotome guided by the intracardiac finger was passed up through the obstruction out into the pulmonary artery; after dividing the stenosis the instrument was removed and the finger was passed up into the pulmonary artery as a dilator. In case of a lower infundibular stenosis a pair of modified bone rongeurs was plunged into the heart, jaws open to engage the septum. A good-sized bit of tissue was thus removed, usually widely interrupting the continuity of the obstructing septal wall. In the three cases of localized constriction in the main pulmonary artery dilatation with graduated urethral sounds seemed to enlarge the arterial lumen satisfactorily. There were seven deaths (a mortality rate of 23.3%), three in the group of patients with valvular stenosis, and four in the group with infundibular stenosis. This mortality rate, although high, is consistent with the early results obtained with anastomotic procedures. The most disconcerting intraoperative complication was cardiac arrest; this occurred in 12 patients, but 8 of these recovered by the use of proper measures. In the immediate postoperative period the most challenging complication were signs of cardiac failure. In spite of the disappointing results in some patients and the complications in others it must be concluded that the direct intracardiac approach to the problem of pulmonary stenosis, whether it be pure or a part of tetralogy of Fallot, appears to be sound and logical from both the anatomic and physiological standpoints. The direct approach, if technically feasible, would appear to offer a more satisfactory long-term solution than the currently accepted anastomotic procedures for the relief of pulmonary stenosis in the tetralogy of Fallot, which are attended by certain dangers because an additional vascular defect has been produced.

Coronary Artery Insufficiency.—Animal experiments showed that when the internal mammary artery is placed in the ventricular myocardium, it forms new arterial branches that anastomose with the left coronary circulation. When this occurs, the heart is protected against death by infarction following the occlusion of the anterior descending branch of the left coronary artery. An internal mammary coronary artery anastomosis had functional value. It relieved artificially produced coronary artery insufficiency. The implant procedure differs from other grafting operations in that the internal mammary artery is not placed on the surface of the heart but is pulled into position by blunt dissection between the heart muscle fibers. Little damage is done to the heart muscle fibers and almost no reaction occurs around the implanted artery. The implanted artery, when it forms an anastomosis, furnishes a third artery to the left ventricle beyond the points of coronary artery occlusion. Four men between the ages of 49 and 55 with coronary artery insufficiency were treated by implantation of the left internal mammary artery into the left ventricular myocardium. The operative procedure appeared to cause no disturbance of cardiac function. The first patient operated on died 62 hours after the operation. At necropsy the internal mammary artery, as in the animal, was found to be completely patent. Death was due to a recent thrombosis of the anterior descending branch of the left coronary artery with ventricular infarction. The author believes that coronary thrombosis developed because of the continuous low blood pressure that was present throughout the operation. In order to bring these patients through an intrathoracic operation without further damaging their coronary artery system, it is necessary to maintain their blood pressure throughout the entire operative procedure. The three other patients in whom blood pressure was maintained by means of a continuous drip of phenylephrine hydrochloride survived the operation. One was well and working after five months, and the others showed improvement. There was no evidence that the procedure caused any harm to the existing coronary circulation.

Kansas Medical Society Journal, Topeka

53:1-44 (Jan.) 1952

*Primary Carcinoma of Lung: Study of 120 Autopsied Cases. D. M. Gibson.—p. 1.
Strangulated Partial Enterocele (Richter's Hernia) Within Femoral Canal: Report of Two Cases Treated by Resection and Primary Anastomosis of Bowel. C. D. Enna and E. Guy.—p. 4.
Infarction of Right Ventricle: Report of Case. A. Pollak.—p. 8.
Errors in Diagnosis: How Made and How Avoided. R. Gorrell.—p. 10.

Carcinoma of Lung.—In 12,812 necropsies performed over a 35 year period at the Kansas Medical Center, malignant growths were found in 1,840 cases, including 120 cases of primary carcinoma of the lung. Thus, primary carcinoma of the lung occurred in 0.9% of all autopsies and in 6.5% of all cases of malignant growths. It is exceeded in frequency by sarcomas, intracranial tumors, and carcinomas of the stomach, colon, and prostate. There has been both an apparent and a real increase in the incidence of carcinoma of the lung in recent years. The mean age was 54, with an age range of 29 and 89 years, and 85% of the lung carcinomas occurred in men. They were found in a hilar region in 92% of the patients. Distant metastases were noted in 86% of the cases, and the liver, adrenals, brain, bones, heart, and kidneys were most frequently involved. Cough was the commonest presenting symptom, followed by dyspnea, chest pain, and hemoptysis. Of 19 cases with brain metastasis, the presenting symptoms of 13 were due to the intracranial lesion. The tumors were classified as follows: squamous cell carcinoma, 48 cases; adenocarcinoma, 42 cases; and anaplastic carcinoma, 30 cases. Well-differentiated squamous cell growths show less tendency to metastasize than other types, while differentiated adenocarcinomas behave much as anaplastic tumors do.

Medical Annals of District of Columbia, Washington

20:641-700 (Dec.) 1951

Medicine—Its Present and Future Problems. L. H. Bauer.—p. 641.
Emotional Stresses in the World Crisis. W. Overholser.—p. 645.
Trauma and Primary Brain Tumor. J. A. Wagner.—p. 650.
Surgery of Anus. W. S. McCune.—p. 653.
*Employability of Epileptics. I. L. Berman.—p. 658.
Heart Block in Pregnancy: Report of Two Cases. J. R. Epstein and H. E. Altman.—p. 660.

Employability of Epileptics.—The 7,000 employees of the United States Government Printing Office include persons with various types of handicaps, such as deaf persons, some with healed tuberculosis, amputees, and 11 or more with epilepsy. The United States Civil Service Commission does not reject epileptics for sedentary or desk positions, provided "the person is under medical supervision and the disease is well controlled." Some epileptics try to hide their illness, but when they learn that the medical staff is ready to help them, they are anxious to unburden themselves. Those who are not adequately controlled and have grand mal seizures are immediately taken off hazardous work

and reassigned to nonhazardous jobs. Four case histories are cited to illustrate experiences with epileptic employees. The seizures of all 11 epileptics are well controlled with various medications. Gainful employment is unquestionably one of the best therapies.

Metabolism, New York

1:1-100 (Jan.) 1952

Incorporation of Glycine Nitrogen into Uric Acid in Normal and Gouty Man. J. D. Benedict, M. Roche, T. F. Yü and others.—p. 3.
Origin of Urinary Creatine in Progressive Muscular Dystrophy. M. Roche, J. D. Benedict, T. F. Yü and others.—p. 13.
*Utilization and Protein-Sparing Action of Fructose in Man. A. A. Albanese, W. C. Felch, R. A. Higgons and others.—p. 20.
Thyroid Function in Normal and Pathological States as Revealed by Radioactive Iodine Studies: I. Thyroid I^{131} Uptake and Turnover in Euthyroid, Hyperthyroid and Hypothyroid Subjects. A. S. Freedberg, D. L. Chamovitz and G. S. Kurland.—p. 26.
Id.: II. Factors Influencing Uptake and Turnover of I^{131} by Thyroid Gland. A. S. Freedberg, D. L. Chamovitz and G. S. Kurland.—p. 36.
*Influence of Potassium on Tissue Protein Synthesis. P. R. Cannon, L. E. Frazier and R. H. Hughes.—p. 49.
Changes in Nutritional Requirements Accompanying Marked Changes in Hormone Levels. J. Meites.—p. 58.
Influence of Food Intake on Ketosis, Mineral Balance and Survival of Alloxan-Diabetic Rats. W. A. Brodsky, N. Nelson and G. M. Guest. —p. 68.
*Fat Emulsions for Oral Nutrition: IV. Metabolic Studies on Human Subjects. T. B. Van Itallie, W. B. Logan, R. L. Smythe and others. —p. 80.
Metabolism Cage for Rats, with Feeding Device that Minimizes Food Scattering. G. M. Guest, W. A. Brodsky and N. Nelson.—p. 89.

Utilization and Protein-Sparing Action of Fructose.—A comparison was made between the metabolism of intravenously administered 10% invert sugar solution and that of 10% dextrose solution in five fasting convalescing men. During the infusion of invert sugar the total blood sugar level rose more rapidly initially than during the infusion of dextrose, but did not reach as high a peak. This suggests that intravenously administered fructose is more readily metabolized than dextrose and presumably induces a more rapid glycogenesis. During and after invert sugar administration only 0.5% to 2.1% of the total sugar administered was lost in the urine, as contrasted with 10% to 26% following dextrose administration. Apparently invert sugar infusions result in negligible loss not only of fructose but also of dextrose. There was 50 to 80% less diuresis in patients receiving invert sugar. In postoperative patients metabolism of invert sugar was unimpaired but dextrose seemed to be utilized less efficiently, as indicated by higher blood sugar levels during infusion. Studies with orally administered sugars in four normally growing children demonstrated that diets in which approximately 70% of the total carbohydrate was fructose induced a marked increase in nitrogen retention in each case. This result was not achieved with diets high in dextrose or galactose. The protein-sparing action of the high fructose diet was diminished when there was an isocaloric reduction of daily protein nitrogen intake from a normal value of 300 mg. per kilogram of body weight to 200 mg. per kilogram. Diets containing 250 to 300 gm. of fructose per day had little or no effect on blood sugar levels and caused negligible fructosuria, indicating that fructose is as physiologic a sugar as dextrose. The authors conclude that invert sugar infusions offer the following practical advantages over dextrose infusions: (1) They provide a readier source of energy than glucose for periods of severe metabolic stress, and (2) their greater protein-sparing effect should reduce undesirable nitrogen losses usually induced by accidental or surgical trauma.

Potassium in Tissue Protein Synthesis.—In parenteral feeding the intracellular electrolytes were formerly largely disregarded, but it seems possible that the efficiency of parenteral feeding might be considerably improved by supplementation with potassium salts. In the past it was difficult to study potassium deficiency because the experimental diets contained protein, which varied in its potassium content. Now it is possible, however, to satisfy the nutritive needs for nitrogen by a mixture of amino acids that contain no potassium. Experiments designed to determine the influence of dietary potassium on the processes of tissue protein repletion indicated that this intracellular cation is essential in the reconstruction of tissue protein. Whereas in protein-depleted rats a repletion ration affording an adequate supply of calories, vitamins, amino acids, and salts caused effective recovery of lost weight, removal of potassium from the salt mixture in the ration led to poor food consumption, failure to gain weight adequately, development of cardiac lesions characteristic of potassium deficiency, and early death. However, addition of small amounts of potassium chloride to the deficient ration enabled the animals quickly to achieve effective protein repletion. Experiments also revealed the inability of two protein hydrolysates of excellent amino acid composition to accomplish effective protein repletion in the absence of potassium salts in the basal ration. This indicates the need for potassium supplementation when these hydrolysates are to be used in parenteral feeding.

Fat Emulsions for Oral Nutrition.—Recently a fat preparation was described that is reasonably palatable and contains more calories than conventional dietary supplements. The emulsion contains 40% fat and 10% dextrose. It provides 4 calories per gram (1,000 calories in an 8 oz. [250 cc.] glass) in contrast to the 1.4 calories per gram supplied by a rich egg nog. Its palatability appears to be due to the small size of its fat particles, most of which are below 1 μ in diameter. Therapeutic amounts of the preparation were well tolerated in 85% of 250 patients and volunteers. This report describes metabolic studies on four persons who tolerated 250 to 550 cc. of the preparation, providing 1,000 to 2,200 calories per day. Nitrogen and potassium deficits due to a calorically inadequate diet were corrected by the emulsion. Fat balance studies on three subjects showed that the ingested fat was well assimilated. In one subject fat emulsion given by mouth caused more efficient utilization of marginal amounts of intravenously administered nitrogen. Although the oral fat emulsion was well accepted by these four subjects, previous clinical experience indicates that a small incidence of intolerance must be anticipated. There is no evidence that emulsification per se enhances the intestinal absorption of fat; in fact, it has been shown that emulsified preparations of this kind are unstable in the rat stomach and intestine. Clinical use of the oral fat emulsion must take into account the vagaries of the gastrointestinal response to fat in any form.

Minnesota Medicine, St. Paul

34:1133-1234 (Dec.) 1951

The Changing Mole. S. W. Becker.—p. 1153.
Congenital Obstruction of Alimentary Canal in Newborn. D. P. Anderson and R. R. Wright.—p. 1159.
*Use of Adrenocorticotrophic Hormone in Treatment of Myasthenia Gravis. S. K. Shapiro.—p. 1160.
Unresolved Pneumonia. H. H. Joffe and S. E. Silvertson.—p. 1165.
Botanical Consideration of Weed Oleoresin Problem. S. Mackoff and A. O. Dahl.—p. 1169.
Repair of Ventral Hernia with Knitted Wire Mesh. C. T. Eginton and J. A. Henderson.—p. 1174.
Ventricular Aneurysm: Case of More than 12 Years' Duration. H. H. Hanson and H. L. Smith.—p. 1177.
Endocrinogenic and Neurogenic Factors in Hypertension. J. J. Eustermann.—p. 1181.

Corticotropin in Treatment of Myasthenia Gravis.—With the introduction of corticotropin it was hoped that patients with myasthenia gravis might be helped. Less than 30 cases of myasthenia gravis have been reported to date in which corticotropin was used, and observations indicate that corticotropin is not a panacea for these patients. Its use is not without danger but nevertheless some patients have obtained definite improvement. In the first of the three patients reported here the administration of corticotropin during an acute phase of the disease appeared to cause a worsening. Subsequently a partial remission developed. Following a second course of corticotropin there was a definite improvement and the patient had an amazing remission which has persisted for one year. In the second patient, the myasthenia gravis became progressively more severe, until she had an acute exacerbation during which tracheotomy and respirator care were necessary. The patient became prostigmine-fast. Her condition remained exceedingly precarious for nearly a month, and at the end of this time she apparently began a spontaneous remission. The corticotropin was administered when the patient was in a partial remission and at the time of this report had produced no appreciable effect. The role of corticotropin in prolonging her remission will be difficult to determine. The third patient was

growing progressively worse at the time corticotropin administration was commenced. The corticotropin did not alter the course of her disease, and the patient died on the 13th day of corticotropin therapy. Postmortem examination revealed bilateral bronchial pneumonia and a substernal thymoma.

New England Journal of Medicine, Boston

245:997-1032 (Dec. 27) 1951

John Homans Lecture. D. C. Elkins.—p. 997.
Effects of ACTH on Induced Malaria in Man. E. H. Kass, Q. M. Geiman and M. Finland.—p. 1000.
Microsporosis of Scalp: Evaluation of New Therapeutic Agent. B. Appel, M. J. Tye, W. Halpern and D. Paci.—p. 1003.
Chills and Fever Following Oral Use of Procaine Amide (Pronestyl). S. Leibowitz.—p. 1006.
ACTH and Cortisone in Treatment of Ocular Disease. R. W. Smith Jr. and E. H. Steffensen.—p. 1007.

New Orleans Medical and Surgical Journal

104:253-296 (Jan.) 1952

Tuberculosis Problem in Louisiana. S. Jacobs, A. A. Calix, M. Campagna and C. C. Kuehn.—p. 253.
Extrathoracic Initial Symptoms in Bronchogenic Carcinoma. C. Oderr. —p. 255.
Nonhormonal Carcinoma of Adrenal Cortex. P. L. Getzoff.—p. 258.
Management of Complications of Heart Failure. A. M. Goldman.—p. 261
Present Day Indications for Cesarean Section: Report of Cesarean Sections Performed on the Tulane Service at Charity Hospital, January 1, 1949—January 1, 1951. I. Dyer and F. Gilbert.—p. 266.
Kirschner Wire Intramedullary Fixation Versus Hanging Case in Fracture of Humerus. J. E. Wheeler.—p. 271.
Clinical Features of Acute Gastroenteritis, Presumably Viral in Etiology. S. G. Wolfe and C. H. Webb.—p. 273.
Premalignant Lesions of Colon. J. H. McCormick Jr.—p. 279.
Common Dermatological Problems in Refining of Petroleum. H. Hansen, E. R. Hawkins, M. E. Kopfler and J. LaNasa.—p. 280.

Ohio State Medical Journal, Columbus

48:1-96 (Jan.) 1952

Compulsory Hospital Isolation of Recalcitrant Positive—Sputum Patient (with Analysis of Extremely Successful Enforcement Plan). W. L. Potts and O. M. Goodloe.—p. 25.
*Treatment of Primary Atypical Pneumonia—Need for Controls in Evaluation of Aureomycin Therapy. I. G. Tillotson and R. O. Oseasohn. —p. 32.
Woman's Hazards in Business, Politics and Industry. A. Ruppersberg Jr. —p. 34.
Hemipelvectomy: Experiences with Three Cases. F. J. Rack and J. H. Lazzari.—p. 38.
Treatment of Epilepsy—(Report on Results of Treatment of 51 Students Attending Ohio State University). N. Michael.—p. 42.
Perforated Peptic Ulcer of Stomach and Duodenum. C. R. Lulenski. —p. 44.

Aureomycin in Primary Atypical Pneumonia.—Three series of cases of primary atypical pneumonia treated with aureomycin that were reported with controls were summarized by Tillotson and Oseasohn as follows: (1) Schoenback and co-workers observed what appeared to be a significant reduction in duration of fever in aureomycin treated patients, but the control and treated series are of questionable comparability in that the patients of each group were observed in different years; (2) Harvey and coworkers presented a small series of alternate treated and untreated patients, in which no difference between the two was apparent; (3) Meiklejohn and Shragg observed some reduction in duration of febrile period in their aureomycin treated patients. The control series showed a much higher incidence of cold hemagglutinin titers than did the treated series. This suggests the possibility that the untreated cases had more severe disease than the treated cases for the following reasons: the titer of cold agglutinins appears to be directly related to the severity of the disease, and the data presented in the other reports give no indication that aureomycin treatment suppresses the formation of this antibody. Analysis of the data presened reveals few, if any, adequately controlled observations, so that the specific effectiveness of aureomycin cannot be accepted without reservation. Failure of aureomycin to alter the course of primary atypical pneumonia in a few patients appears highly significant in the absence of controlled studies. Final judgment regarding effiicacy of aureomycin in primary atypical pneumonia must be withheld despite several enthusiastic clinical reports.

Proc. Soc. Exper. Biol. & Med., Utica, N. Y.

78:665-886 (Dec.) 1951. **Partial Index**

*Preparation of Clinically Active Adrenocorticotropic Hormone (ACTH) in Good Yield from Sheep Pituitary Glands. Choh Hao Li, G. W. Liddle, W. O. Reinhardt and L. L. Bennett.—p. 665.
Excretion of Amino Acids in Cystinuria. W. H. Stein.—p. 705.
*Coramine (Nikethamide) as Adjuvant to Atropine in Treatment of Poisoning by EPN (Ethyl p-Nitrophenyl Thionobenzenephosphonate). V. DiStefano, L. Hurwitz, W. F. Neuman and H. C. Hodge.—p. 712.
Plasma Antihemophilic Activity Following Total Body Irradiation. G. D. Penick, E. P. Cronkite, I. D. Godwin and K. M. Brinkhous.—p. 732.
Study of Moniliasis in Aureomycin Therapy. L. V. McVay Jr. and D. H. Sprunt.—p. 759.
Hemolytic Action of Gramicidin and Tyrodicin. K. P. Dimick.—p. 782.
Stabilizing Action of Glycerine on Hemagglutination of Egg-Adapted Mumps, Newcastle Disease and Influenza Viruses. V. J. Cabasso, F. S. Markham and H. R. Cox.—p. 791.
Beneficial Effects of Liver on Cortisone Acetate Toxicity in Rat. B. H. Ershoff.—p. 836.
Hypoproteinemia as Protection in Mercuric Chloride Poisoning. H. F. Martin and N. H. Reid.—p. 863.

Corticotropin from Sheep Pituitary.—Methods previously employed for the extraction of corticotropin from sheep and swine pituitaries produced comparatively low yields. This paper describes a simple procedure that produces from whole sheep pituitaries a much higher yield of purified corticotropin, substantially free from growth, gonadotropic, thyrotropic, antidiuretic, and pressor activities. Clinical and laboratory evidence indicates that corticotropin prepared by this method is therapeutically and metabolically effective in patients with rheumatoid arthritis.

Nikethamide in Poisoning by Organic Phosphates.—A number of organic phosphates such as ethyl *p*-nitrophenyl thiobenzenephosphonate (EPN) have great economic importance as insecticides. Since these compounds inhibit cholinesterase, they are extremely hazardous and the search for efficacious antidotes is important. At present, atropine because of its powerful parasympatholytic activity is the drug of choice in the treatment of poisoning by these agents. It is believed that death following organophosphate poisoning results from respiratory failure. The administration of a respiratory stimulant, then, would seem to be advantageous. Studies reported in this paper proved that the administration of nikethamide (coramine®) and atropine together was considerably more effective in the treatment of ethyl *p*-nitrophenyl thiobenzenephosphonate poisoned rats than was atropine alone. The authors admit, however, that observations on rats cannot be directly applied to the treatment of poisoning in human subjects.

Science, Washington, D. C.

115:1-24 (Jan. 4) 1952. **Partial Index**

Life Span of Leucocytes in the Human. D. L. Kline and E. E. Clifton. —p. 9.
*DDT Resistance in Korean Body Lice. H. S. Hurlbut, R. M. Altman and C. Nibley Jr.—p. 11.
New Method for Detecting Penicillinase Production by Staphylococci. A. A. A. El Ghoroury.—p. 20.
Decrease of Albumin Concentration of Human Blood Serum During Heat Inactivation. P. Koets.—p. 21.

DDT Resistance in Korean Body Lice.—Despite routine application of 10% DDT powder to Korean military personnel, the percentage of persons infested with body lice (Pediculus humanus corporis) increased steadily during the winter and spring of 1951. The method used was essentially that employed by Soper and associates in 1943, except that power dusters were used. The dust is applied without the removal of clothing. The DDT came from various sources, including a large stock of an American manufacture that had been in storage for five or six years. Tests with mosquito larvae, however, demonstrated that it had retained its full potency. After describing various experiments that were carried out with DDT powders and with cloth that had been impregnated with DDT, the authors say that since 1947 DDT resistance in houseflies has been reported from numerous localities where DDT has been in use. Laboratory experiments have demonstrated that resistant strains of flies can be developed by selective breeding, and this has been interpreted as indicating that such a process occurs in nature. It seems probable that an analogous condition exists in the body louse. Hitherto, great dependence has been placed on DDT for the control of typhus; but it now appears to be of uncertain value.

FOREIGN

Acta Chirurgica Scandinavica, Stockholm

102:241-320 (No. 4) 1951. **Partial Index**

Infrapapillary Carcinoma of Duodenum. A. Odelberg.—p. 241.
*Rectosigmoidectomy for Hirschsprung's Disease. T. Ehrenpreis.—p. 251.
*Frequency of Recurrence of Calculi in Gallbladder After Cholecystolithotomy. M. Pers and H. Baden.—p. 260.

Rectosigmoidectomy for Hirschsprung's Disease.—Rectosigmoidectomy by Swenson's technique with two minor modifications was performed on 18 boys and 2 girls with Hirschsprung's disease. The diagnosis of this disease, which is characterized by agenesis of the myenteric plexus within a narrow distal segment of the bowel, depends on the roentgenologic demonstration of such a segment. In the author's cases three types of narrowing of the distal segment were observed as follows: In some cases the entire segment was pronouncedly contracted. In other cases the segment per se appeared to be almost normal, but, when it was compared to the dilated bowel above, there was a pronounced difference in size. In a third group a proximal part of the distal segment was contracted, but the terminal part appeared to be of normal size. The length of the narrow distal segment varied considerably, and there was no correlation between the absolute length of the distal segment and the proportion of the bowel involved. There were no deaths in this series. Except for one partial failure of the surgical intervention due to incomplete resection, all patients obtained complete relief from their symptoms for follow-up periods of from six months to two and one-half years. There have been no strictures of the anastomosis. All patients had normal sphincter control and normal bladder function. The anastomosis broke down in two cases, apparently because of circumscribed necrosis of the proximal segment, which had been deprived of an adequate blood supply. In these cases colostomy was followed by rapid improvement. The importance of a careful check of arterial pulsations in the resection area has been stressed.

Recurrence of Calculi in Gallbladder.—Among 504 patients followed for an average of 19.7 years after cholecystolithotomy, unquestionable recurrence of calculi was demonstrated by reoperation, postmortem examination, or cholecystography in 109 (21.6%), but the actual percentage of recurrences may be assumed to be 30%. Of the 109 patients, 86 had recent symptoms of biliary tract disorder, 15 had no symptoms, while reliable clinical information was not available in the remaining 8 patients. Biliary colic occurred in 42 patients who had no recurrent calculi. In some of the patients recurrent calculi were manifested more than 20 years after the cholecystolithotomy. The highest percentages of recurrence were demonstrated in patients less than 40 years old, in those with the least significant changes in the gallbladder, and in those with uninfected gallbladder contents. There thus appeared to be a great risk of recurrent calculi in patients whose gallbladders seemed suitable for preservation. Women showed a greater tendency to recurrence than men, which conforms with the fact that biliary calculi develop more frequently in women than in men. The lowest incidence of recurrent calculi was observed among patients who had gallstones removed not only from the gallbladder but also from the common and cystic ducts.

British Journal of Dermatology, London

63:431-488 (Dec.) 1951

Pigmentation of Skin. J. H. Burn.—p. 431.
*Pineapple Dermatosis. I. Polunin.—p. 441.

Pineapple Dermatosis.—In Hawaii the pineapple industry has long been highly mechanized. Handling of pineapples is reduced to a minimum, and contact with the juice is prevented by rubber gloves. The "pineapple burn," as it is called, is rarely seen in Hawaii today. In Malaya the fruit is usually cut by hand for canning. In this work the hands are exposed to the juice in spite of the use of rubber gloves. At the beginning of the canning season dermatitis develops in the workers, and is worst on pressure areas. The hands are tender for the first few days, when raw areas are often seen on the finger tips. The condition later becomes painless, and this is ascribed to the development of an opaque white appearance of the skin. Biopsy specimens show an almost complete disappearance of the stratum granulosum, which becomes a poorly defined layer that contains few granules and consists of cells widely separated by an increase of intercellular fluid. The stratum corneum shows evidence of stratification and the Malpighian stratum is probably thickened. The horny ridges, and hence the fingerprints, become temporarily obliterated. Bromelin, the proteolytic enzyme from pineapple, causes the same lesions as pineapple juice when rubbed on to the skin, and is thought to be the cause of the dermatosis. Proteolytic enzymes cause separation of the superficial layers of skin and increase skin and capillary permeability. The action of proteolytic enzymes on the skin was not prevented by the use of high concentrations of an antihistamine drug.

British Medical Journal, London

1:59-118 (Jan. 12) 1952

Physiology and Relief of Traumatic Arterial Spasm. J. B. Kinmonth.—p. 59.
Simple Standard Exercise Test and Its Use for Measuring Exertion Dyspnoea. P. Hugh-Jones.—p. 65.
Late Results of Perurethral Prostatic Resection. T. L. Chapman and J. W. Sutherland.—p. 72.
Incontinentia Pigmenti: Report of Case, with Summary of 29 Cases from Literature. A. W. Franklin.—p. 75.
Congenital Duodenal Obstruction and Mongolism. M. Bodian, L. L. R. White, C. O. Carter and J. H. Louw.—p. 77.
Acute Infectious Lymphocytosis: Report on Group of Cases in a Day Nursery. H. G. Dunn.—p. 78.
Tuberculous Meningitis: Treatment with Streptomycin and Para-Aminosalicylic Acid. S. R. Jamieson.—p. 83.
Chloramphenicol in Treatment of Cutaneous Anthrax. P. S. Clarke.—p. 86.
Bleeding Meckel's Diverticulum: Report of Two Cases. J. N. Walton and N. D. Lill.—p. 88.

Doc. Neerland. et Indon. de Morbis Trop., Amsterdam

3:289-384 (No. 4) 1951. **Partial Index**

Control of Hyperendemic Malaria in Java, Caused by A. Sundaicus, by DDT House-Spraying. P. H. van Thiel and R. M. P. Winoto.—p. 295.
Tropical Eosinophilia and Filariasis. J. H. Reisel and J. Groen.—p. 320.
Epidemiological Aspect of Malaria in Equatorial Africa. N. H. Swellengrebel.—p. 325.
*Treatment of Hepatic Abscess with Chloroquine. J. J. C. P. A. Roovers and P. B. van Steenis.—p. 333.
Healthy Pigs as Salmonella Carriers in Java; Aerobic Bacterial Flora of Their Mesenteric Lymph Nodes. F. C. Kraneveld, M. Erber and M. Mansjoer.—p. 343.
Incidence of Cancer in Indonesia. W. Kouwenaar.—p. 357.

Chloroquine Treatment of Hepatic Abscess in Amebiasis.—Roovers and Steenis discuss the drugs that have been used in the treatment of amebiasis and particularly of hepatic abscess resulting from amebiasis. The results of drug therapy of amebiasis depend on the amebicidal effect of the drug, which in turn depends on the concentration of the drug at the sites where the ameba are present: in the intestinal wall, liver and other tissues as histolytical forms, and in the intestinal lumen as cystic forms. Chloroquine had a rapid action and gave good results of long duration in four patients. Two who had proved refractory to emetine have been free from relapses for 18 months to 2 years. A course of chiniofon or carbarsone should be given after termination of chloroquine (or emetine) treatment of the hepatic abscess in order to destroy the cysts in the intestinal lumen.

East African Medical Journal, Nairobi

28:397-448 (Oct.) 1951. **Partial Index**

*Treatmem of Tick-Borne Relapsing Fever in East Africa with Special Reference to Aureomycin. H. C. Trowell.—p. 403.
Surgical Emphysema of Intestine After Gastro-Enterostomy. C. J. S. Sergel.—p. 413.
Medical Missionary Work in West Nile District of Uganda. E. H. Williams and P. H. Williams.——p. 415.
Leprosy in Teso District, Uganda. H. W. Wheate.—p. 420.

Aureomycin in Relapsing Fever.—The consensus is that the arsenicals are useless if not dangerous in tick-borne relapsing fever as seen in East Africa, although they may be of some use in louse-borne relapsing fever. While penicillin may shorten the acute attack, it does not prevent relapses. Trowell feels that the

more favorable effects of arsenic and penicillin reported by some investigators may be explained by the fact that in other parts of the world the spirochete strain may be different. Since aureomycin was quite effective in treatment of tick-borne relapsing fever in Africans at the Witwatersrand mines and in patients with this disease in Portuguese West Africa, Trowell decided to investigate the effect of this drug on tick-borne relapsing fever in a controlled study. Alternate patients were placed either in the control group, which were untreated except by 10 gr. (0.6 gm.) of aspirin three times a day, or in the group who were given aureomycin. Relapses occurred in 8 of 13 control cases, and two children who were seriously ill and had relapsed several times were transferred to the aureomycin group, with prompt relief of their symptoms. The mean duration of the febrile period of the first bout of fever in the control group was 50 hours, and spirochetes were detected in the blood smears for a mean period of 24 hours. Aureomycin was given to 14 patients, including the two children transferred from the control group. No relapses were observed in the subsequent afebrile period, which in 11 cases exceeded 10 days. The mean duration of the febrile period of the first bout of fever was 11 hours, and spirochetes usually disappeared within three hours of aureomycin administration. The average minimal effective dose was 2 gm. and may be smaller. Subsequent to this investigation cure was obtained in two more cases of relapsing fever following administration of only 0.5 gm. of aureomycin, and in both cases the blood smear became negative within two hours.

J. Franç. Méd. et Chir. Thorac., Paris

5:509-604 (No. 6) 1951. **Partial Index**

Mechanism of Emphysema Surrounding the Pneumonoconiosis Lesions Caused by Coal Dust. A. Policard.—p. 509.
Constrictive Pericarditis; Etiology; Histories of Four Cases of Tuberculous Pericarditis, Two of Which were Constrictive. E. Stephan. —p. 512.
*Note on 400 Cutaneous Histoplasmin Tests Performed in Children. P. Fréour and Arnoux-Laujac.—p. 576.

Cutaneous Histoplasmin Tests in Children.—Cutaneous histoplasmin tests were performed on 417 children by injecting subcutaneously in the deltoid region 0.1 cc. of a 1% solution of histoplasmin. Readings were made 48 hours later. Four children who were anergic to Pirquet and Mantoux tests had reactions to histoplasmin 5, 6, 6, and 7 mm. in diameter. Reactions to simultaneous tests with coccidioidin were likewise positive. These children were receiving rest treatment because of general fatigue. Clinical examinations did not reveal any abnormality. Roentgenologic examinations of the lungs disclosed no abnormalities. Six children had a reaction to histoplasmin greater than 6 mm. in diameter, but they also showed a strongly hyperergic reaction to tuberculin. They probably had a primary tuberculous infection, and three had the lymph node and osteoarticular manifestations. Two other children had positive reactions to histoplasmin of unspecified diameter. One, a child aged 5, had scrofulous lesions with a vesicular Pirquet's reaction; the other, aged 9, had arthritis of the right knee and was anergic to tuberculin. Roentgen examination of the lung did not reveal any abnormality. All of the remaining children reacted negatively to histoplasmin. It was not concluded that the children with a positive reaction to histoplasmin had histoplasmosis, since this reaction is not always specific. A strongly positive reaction to histoplasmin frequently coincides with a strongly positive reaction to coccidioidin or tuberculin, as in the authors' cases. The authors' results suggest that additional tests, such as complement fixation, flocculation, and particularly detection and culture of parasites from the blood or bone marrow may be required for the diagnosis of histoplasmosis.

Journal of Laryngology and Otology, London

65:809-876 (Dec.) 1951

Treatment of Maxillary Sinusitis by Local Injection of Procaine Penicillin-in-Oil. M. S. Strong and R. W. Tonkin.—p. 809.
Sympathectomy and Internal Ear. R. S. Lewis.—p. 825.
The Hearing of Undergraduates: Pilot Study Using Audiometry. R. W. Parnell.—p. 843.
Case of Boeck's Sarcoidosis of Cervical Lymph Glands. H. M. Parsons and W. McKenzie.—p. 848.

Medical Journal of Australia, Sydney

2:833-868 (Dec. 22) 1951

Time, Science and the Individual. D. J. Thomas.—p. 833.
Survey of Incidence of Interdigital Tinea in Group of Students from the University of Queensland. B. T. Emmerson.—p. 837.
Investigations into Aetiology of Glomerulonephritis: Preliminary Report. D. Bialestock.—p. 842.
Research in Physical Education and Related Subjects, with Special Reference to University Departments of Physical Education. F. Duras. —p. 846.
Curare and Electro-Convulsive Therapy: Simplified Technique. R. R. Webb.—p. 851.
Determination of Sodium and Potassium in Blood Serum. O. E. Neufeld. —p. 851.

2:869-892 (Dec. 29) 1951

Criteria of Cancer Cure. W. E. Gye.—p. 869.
Importance of Relativity of Blood Pressure and Other Signs in Prevention of Eclampsia. T. D. Hughes.—p. 871.
*Iron Losses of Healthy Women During Consecutive Menstrual Cycles. J. Millis.—p. 874.

Iron Losses During Menstruation.—The fact that the hemoglobin level in women can be raised to that in men by administration of iron salts suggests the presence of some degree of anemia in women. The anemia may be due to a lower dietary intake of iron, to less efficient absorption and utilization, or to a greater loss of iron from the body than in men. Each of these possibilities is considered in this paper in the light of published work and of the information obtained from this study on 14 student nurses in a Melbourne hospital. Each subject was given a thorough examination at the beginning of the experiment. Blood samples were withdrawn for hemoglobin estimation each week. The menstrual flow was collected on cotton pads. Iron intake was calculated from records of food consumption. The percentage of hemoglobin in blood in each subject varied from week to week, but there was no consistent relationship between hemoglobin levels and the duration of the menstrual cycle. Furthermore, the iron losses in a subject varied from one menstrual period to another, which made it necessary to determine the losses on several occasions to obtain a reliable figure. The loss of iron varied from 3.5 to 66.8 mg. of iron per menstrual period, and the average for 57 menstrual periods was 21.8 mg. Four of the 14 persons studied require 1 mg. or more of iron per day to replace the loss in menstrual fluid. Therefore at least 2 mg. of iron would have to be absorbed each day to replace the losses in urine, feces, bile, and menstrual fluid. On the basis of information available at present, women who have to replace iron from menstrual loss at the rate of less than 1 mg. per day can do so if they have an adequate diet. However, further studies are required to show whether larger amounts of iron can be absorbed, as will be necessary for some women who have higher losses. It seems likely that a gradual depletion of the iron stores will occur in these women and may eventually be reflected in their hemoglobin level.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

95:3621-3716 (Dec. 8) 1951. **Partial Index**

Treatment of Aneurysm of Abdominal Aorta. I. Boerema.—p. 3622.
*Diagnosis of Bronchial Carcinoma: Results of Cytologic Examinations of Bronchial Secretion. B. K. S. Dijkstra.—p. 3627.
Combination of Developmental Disturbances in Region of Umbilicus. J. Hage.—p. 3636.
*Vitamin B_6 in Treatment of Epilepsy. W. Ernsting and T. P. Ferwerda. —p. 3643.

Cytological Examination of Bronchial Secretion.—The cytological examination of the bronchial secretions of 198 patients revealed bronchial carcinoma in 34. Fourteen of these were revealed by the cytological test only. Of 48 bronchial carcinomas finally found, only 3 were not detected by the combined anatomic and cytological examination. One false positive test was obtained. The author stresses the advantages of the cytological test, and says that it should be performed whenever there is even the slightest suspicion of bronchial carcinoma.

Pyridoxine in Epilepsy.—Observations on animals having proved that the lack of pyridoxine (vitamin B_6) in the diet leads to development of epileptic attacks, it had been used by some observers in treatment of patients with petit mal and of some who

had both petit and grand mal attacks. This paper reports on the use of pyridoxine in 14 patients from 2 to 17 years old. All had petit mal and one also grand mal epilepsy and had not responded to treatment with various antiepileptic drugs and ketogenic diets. In five of these the attacks disappeared and three others showed improvement, but the other six had no decrease in the number of attacks. The pyridoxine was given in doses of 20 mg. from three to six times a day.

Nordisk Medicin, Stockholm

46:1811-1846 (Dec. 5) 1951. **Partial Index**

Acute Anuria in Connection with Pregnancy. F. Berglund and L. Werkö.—p. 1814.
Age Incidence in Cancer of Uterus: Value of Cytological Investigations. R. Bredland.—p. 1820.
Cancer of Body of Uterus. R. Bredland.—p. 1822.
*Myoma After Menopause. J. A. Abolins.—p. 1825.
Pernicious Anemia, Resistance to Liver and Acquired Hemolytic Anemia. N. Bergqvist.—p. 1828.
"Palindromic Rheumatism." E. Carsten Astrup.—p. 1830.

Myoma After Menopause.—Of the 29,092 patients treated in the gynecologic department of the Sabbatsberg Sjukhus from 1941 to 1950, 1,990 had myomas, and in 113 of these menstruation had ceased a year or more before. Most of them were aged between 51 and 55; the youngest was 44, the oldest, 79. Bleeding, pain, and bladder distress were the commonest symptoms. In 12% the myoma was an accidental discovery. The myomas varied from the size of a goose egg to tumors extending to the xiphoid process. Operation was done in 102 cases; supravaginal amputation, with or without salpingo-oophorectomy, was the method in 59 cases. One death occurred. Abolins says that myomas after the menopause that give rise to symptoms in the form of bleeding, pain, growth, and bladder discomfort should be treated operatively, partly because 15% are malignant or combined with other malignant tumors, partly because the malignancy of the growth cannot be determined without operation and pathological examination.

Prensa Médica Argentina, Buenos Aires

38:3185-3258 (Dec. 7) 1951. **Partial Index**

*Cortisone and Corticotropin (ACTH) in Lupus Erythematosus Disseminatus. J. M. M. Fernández.—p. 3186.
Spontaneous Emphysema of Mediastinum. E. G. Fongi.—p. 3203.
Thiosemicarbazone in Treatment of Some Forms of Cutaneous Tuberculosis. A. A. Cordero and S. O. García.—p. 3224.
Classification of Essential Arterial Hypertension. A. P. Real.—p. 3227.

Cortisone and Corticotropin in Lupus Erythematosus Disseminatus.—During 1951 the author observed 12 cases of lupus erythematosus disseminatus and 10 cases in adults are described here. The disease was acute in the nine women and subacute in the man. All the patients had typical or atypical cutaneous lesions, generalized symptoms suggesting an acute infection associated with anemia, leukopenia, nephritis, arthritis, hepatomegaly, splenomegaly, cervical adenitis, and in some cases axillary and inguinal adenitis. Two patients had pleuritis and pericarditis. Two had pericarditis and peritonitis in two relapses. Three patients had meningitis and two of these had epileptiform crises, delirium, and acute nervous agitation during the last 48 hours before death. Penicillin and streptomycin were administered in the usual doses to four patients. In three cases the patients died either in the course of the first bout or in a relapse following temporary improvement. Only the man with subacute lupus erythematosus is in remission two years after discontinuation of treatment. Six patients had intermittent treatment with cortisone and corticotropin (ACTH). Cortisone was given in an average daily dose of from 60 to 80 mg. up to a total dose of 1 to 3 gm. Corticotropin was given in an average daily dose of 60 to 80 mg. in four divided doses, up to a total dose of 740 mg. The results of treatment were good but transient in all cases. The treatment is symptomatic. Three patients are still under treatment after relapse, and three died during relapse, but the span of life after treatment seemed to be longer than in cases in which the previous usual symptomatic treatment was employed.

Riforma Medica, Naples

65:1241-1268 (Nov. 17) 1951

*Significance of Enlargement of Parotid Gland in Cirrhosis of Liver: Biopsy Study. M. Sposito and R. Cheli.—p. 1250.
Case of Lithiasis in Horseshoe Kidney (Fusion of Kidneys at Upper Pole). A. D'Alessandro.—p. 1253.

Study of Liver and Parotid Gland by Biopsy.—Biopsy of an enlarged parotid gland and of the liver was performed in 10 patients to determine the relationship between the parotid gland and lesions of the liver, and to study the eventual histological differences of the parotid gland in patients with and without hepatic lesions. Six patients had portal cirrhosis, and one each sclerosis of the liver due to chronic brucellosis, sprue, diabetes, and heart decompensation associated with syphilis. Biopsy of the parotid gland was painless and was performed by introducing an aspirating needle, 2 mm. in diameter, through a small incision made in the enlarged area that had been previously anesthetized with a 2% solution of procaine hydrochloride. All biopsies showed hyperplasia, with a slight increase in adipose tissue. The cell structure was not altered. The liver biopsy confirmed the clinical diagnosis in the first six patients. Diffuse small cell infiltrations and increase of the connective tissue that surrounds the lobules were observed in the patient with sclerosis of the liver due to brucellosis. Only small signs of fat degeneration were present in the patients with sprue and diabetes. Hyperplasia of the connective tissue was slight in the patient with heart decompensation. Reactions to the liver functions tests were abnormal in the first seven patients and normal in the others. Only in the patient with heart decompensation was the enlargement of the parotid gland not associated with lesions of the liver, and its pathogenesis is difficult to explain. But, as a rule, hyperplasia of the parotid gland suggests the presence of manifest or concealed hepatopancreatic disturbances.

65:1297-1324 (Dec. 1) 1951

Rheumatic Cardiopathy and Work Activity. S. Caccuri.—p. 1299.
Probable Consequences of Topical Use of Various Antibiotics. N. M. Sciannameo.—p. 1305.
*Eosinophil Response and Thorn's Hematologic Test with Epinephrine in Surgical Patients. S. Amante and M. Mancini.—p. 1310.

Thorn's Test in Surgical Patients.—Thorn's test with epinephrine was used to study the level of circulating eosinophils in 120 patients who submitted to various types of surgical intervention. Epinephrine in doses of 0.3 mg. was administered intramuscularly three to four hours before measuring the fall in eosinophils. In 70 patients whose preoperative level of eosinophils was normal, Thorn's test was carried out only postoperatively. Twelve to 24 hours after the operation pronounced eosinopenia (average fall of 76.5%) was present in 67 patients, suggesting increased adrenocortical activity. Insufficient activity of the adrenal cortex was known to be present in the other three patients in whom the number of eosinophils had remained unchanged. Administration of adrenocortical preparations, while improving their general condition, did not alter the number of eosinophils. In the second group of 50 patients the test was carried out before and after the operation. The preoperative test revealed a normal eosinophil response (average fall of 70.15%) in all patients. Twenty-four hours after the intervention this eosinopenia was still present or had decreased in 44 patients, while in the other 6 the eosinophil level had returned to the values recorded before the preoperative injection of epinephrine. Thorn's test performed in many of these patients induced a further fall in the number of eosinophils, which decreased again when a second test was performed 48 hours after the operation. In those patients in whom the test was performed for the first time 72 hours after the operation, the level of eosinophils (average fall of 74%) indicated that the adrenocortical activity was normal. In both groups the decrease in the number of eosinophils was not proportional to the severity and length of the intervention, and was not influenced by type of anesthesia, age, and sex of the patient. Thorn's test performed preoperatively may be a good preoperative prognostic factor, while the comparison of preoperative and postoperative eosinophil levels may constitute a good postoperative prognostic aid. According to the author, the best procedure is to perform the

entire test preoperatively and only to count the eosinophils after the operation. The prognosis will be favorable if the eosinopenia that was induced by the preoperative injection of epinephrine is still present or has become more pronounced after the operation.

Sang, Paris

22:701-780 (No. 9) 1951. **Partial Index**

*Involvement of Small Vessels in Neonatal Hemorrhages. A. Minkowski. —p. 701.
Hereditary Anomalies of Blood Disorder in Cooley's Mediterranean Anemia. E. Schwarz-Tiene.—p. 713.
New Studies on Electrophoretic Mobility of Leukocytes. S. Bazin and R. Robineaux.—p. 730.
*Morphological and Experimental Studies on Pathogenesis of Acute Myeloid Leukemia: I. Experimental Heterologous Transmission of Acute Human Myeloid Leukemia. F. Mas y Magro.—p. 756.
*Id.: II. Blood Changes Following Experimental Transfusion of Acute Myeloid Leukemia. F. Mas y Magro.—p. 760.

Involvement of the Small Vessels in Neonatal Hemorrhages.—Pathological study of 80 cases of intracranial hemorrhage in premature infants shows that bleeding is chiefly cerebral and that there are numerous small centers of vascular rupture. Measurements show that resistance of small vessels in infants born at term is abnormally high (50 cm. Hg) as compared to that of the adult; in premature infants there is a relative vascular fragility that is proportional to the weight of the infant (10 cm. Hg in one weighing 900 gm.). The effects of various substances given to the mother at the beginning of labor to increase vascular resistance in the fetus have been studied and the acetate of racemic α-tocopherol (given at least an hour before the end of labor) has been found effective. In a series of 105 premature infants whose mothers were given from 600 to 900 mg. of racemic α-tocopherol acetate, vascular resistance was increased and only four intracranial hemorrhages occurred. In a control series hemorrhages occurred in 12. Opinions on the value of vitamin K differ; if the prothrombin level in the newborn is low, it should be systematically given, but its administration alone will not prevent or stop more than a few of the hemorrhages of birth, and supplementary measures are needed. Capillaroscopy in the newborn reveals that the superficial vessels are thick, dilated, and dense at first, gradually becoming filiform from about the 5th to the 10th day. In infants born at term they tend to disappear by the third week, but in premature infants weighing less than 1,800 gm. they can still be seen in the seventh or eighth week. The oral administration of 2 mg. of racemic α-tocopherol acetate daily for three days to the newborn causes the outlines of the vascular network to disappear in from 4 to 5 days instead of 25 to 45 days, and produces, much more rapidly than in the controls, a filiform appearance of the vessels that is due to vasoconstriction, while at the same time vascular resistance is increased from 10 to 20 cm. Hg. The relationship between vasodilatation and vascular fragility in the newborn is clear, and their importance as factors in the hemorrhages of birth should lead to further study of the problem.

Pathogenesis and Transmission of Acute Myeloid Leukemia.—Proof that acute myeloid leukemia is caused by a virus is found, according to Mas y Magro, in the fact that it has been transmitted from man to guinea pigs, and subsequently from guinea pig to guinea pig. Transmission is accomplished when inoculation of leukemic material (either blood or bone marrow) is carried out by subepidermal scarification. Earlier attempts at transmission by injection failed because serum and blood plasma, as well as the secretions and cells of serous cavities, have an inhibiting effect on the leukemic virus. Viruses are known to give constantly positive results when inoculated by scarification. Material obtained by scraping from scarifications in an inoculated guinea pig will transmit the disease to another guinea pig if inoculation is carried out within one or two days. From the third day on transmission does not take place, because the virus has entered the blood and subsequently the bone marrow. Changes in the mesenchymatous cells of the dermis of the host animal also suggest that the loss of transmissive power after the second day results from adaptation of the virus to the metabolic conditions of the host. Changes produced by transmission in the blood and marrow of guinea pigs parallel those in acute human leukemia. No other pathological changes take place in the inoculated animals, except a loss in weight that usually amounts to half the original weight of the animal. About 95% of the test animals die in from 9 to 28 days, whether transmission is from man to animal or from animal to animal.

Blood Changes Following Transmission of Acute Myeloid Leukemia.—The acute granulocytic form of myeloid leukemia, which is always fatal, shows a blood picture of anemia with between 70% and 80% neutrophils and sometimes even more. The number of leukocytes does not exceed 25,000, and moderate leukopenia may occur. The outstanding characteristic is the presence of from 8% to 16% atypical progranulocytes, with peroxidase granules. They are irregularly distributed, often forming a single clump in the nucleus. In guinea pigs inoculated with blood from patients who had acute myeloid leukemia, whether myeloblastic or granulocytic, an extremely acute myeloid leukemia of the granulocytic type developed that was characterized by neutrophilia and the presence of atypical progranulocytes like those in man. The number of leukocytes tended to fall, but leukopenia did not occur. Identification of the progranulocytes depends on the staining of the peroxidases and requires differentiation between the peroxidase granules of the monocytes, which are fine and sometimes irregular, and those of the progranulocytes, which, like those of the neutrophils, are large and dark green. The development in guinea pigs of myeloid leukemia of the acute granulocytic type, although the blood with which they were inoculated came from a patient with the myeloblastic type, suggests that the same virus causes both these types in man.

Schweizerische medizinische Wochenschrift, Basel

81:1291-1312 (Dec. 29) 1951. **Partial Index**

*Surgical Treatment of Focal Epilepsy. G. Weber.—p. 1291.
Cobalt in Treatment of Hypochromic Anemias. H. Dittrich.—p. 1296.
Investigations on Production of Lupus Erythematosis Cells in Normal Blood. T. Inderbitzin.—p. 1298.
Secondary Effects in the Course of Treatment of Tuberculosis with *p*-Aminosalicylic Acid. L. Morandi, H. Ochsner and A. Neuenschwander.—p. 1301.

Surgical Treatment of Focal Epilepsy.—The radical excision of a scar, even if it is apparently the focus of an epileptic attack, is justified only when the lesion produced by the excision is less harmful than the original focus. Weber reviews the results obtained by others, particularly by Penfield, with surgical treatment of focal epilepsy and then reports results obtained at his clinic with the surgical treatment of 88 epileptic patients who were selected from among a total of 1,169 cases. A total of 75 of these 88 were treated before the introduction of electroencephalography, but in the last 13 both electroencephalography and electrocorticography were employed to detect the epileptogenic focus. In 59 of the first group either circumscribed lesion of the brain was found that presumably represented the epileptogenic focus, or electrical stimulation of an area produced an epileptic attack that corresponded to the spontaneous attacks. The epileptogenic focus was excised in 43 of the cases; in the remaining 16 patients only adhesions in the region of the focal lesions were removed because excision did not seem advisable. In 16 other patients no changes could be seen or elicited electrically in the exposed portion of the brain, and no tissue was excised. The epileptogenic focus was found in all of the 13 patients who were operated on under electrocorticographic control, and removal was attempted in 10 of these patients. Summarizing his experiences with the surgical treatment of epilepsy, the author says that a certain percentage of epileptic patients will become completely or at least temporarily free of attacks, and in others the number of the attacks will be reduced. The efficacy of the surgical treatment varies with different investigators, but complete cures are not frequent. Even Penfield, with his great experience, obtained complete freedom from attacks in only about a fourth of those in whom he was able to remove the epileptogenic focus. Weber's results are considerably less favorable, and he feels that surgical treatment should be tried only when the best managed medicinal treatment does not restore the patient to a bearable condition. Furthermore, the epileptogenic focus must not be the result of a diffuse progressive brain lesion. The patient and his relatives should be told that surgical treatment may give relief but the outcome cannot be foretold.

BOOK REVIEWS

Air War and Emotional Stress: Psychological Studies of Bombing and Civilian Defense. By Irving L. Janis. Rand Corporation Series. Cloth. $5. Pp. 280. McGraw-Hill Book Company, Inc., 330 W. 42d St., New York 18; Aldwych House, Aldwych, London, W.C.2, 1951.

This monograph outlines the results of a technical study of the reactions of persons subjected to conventional and atomic bombing during World War II. The study was undertaken to evaluate the psychological effects of air warfare and delineate certain major problems that may arise in planning for the defense of the United States against air attack.

The results are based on a combination of qualitative examinations of individual eyewitness accounts of bombing disasters and analyses of official reaction surveys, such as the United States Strategic Bombing Survey.

Although the evidence presented as to the results of conventional and atomic bombing is too fragmentary for many conclusive deductions, it indicates that overt panic and disorganized behavior occurring in Japan and Europe was localized and that such behavior was not widely prevalent among those who survived. The book indicates that temporary and permanent emotional disturbances were greater among inhabitants of European cities that were heavily bombed than among persons residing in Hiroshima and Nagasaki.

Despite the shortcomings of available evidence, the author concludes that air attacks of the type employed against civilian communities during World War II produced only a slight increase in chronic psychopathological and psychosomatic disorders. Mental breakdown, panic, and mass demoralization rarely materialized during World War II, and, although shock did occur on a sizable scale, most patients recovered fairly rapidly.

If, however, at some future time, large scale A-bomb attacks, as contrasted with the type of bombing employed during World War II, are launched against the United States, it is agreed that the psychological impact upon the American people might prove to be as shattering as the physical devastation. As pointed out by Mr. Janis, the ability of a community to minimize the disorganization and fear caused by air raids will be dependent largely on previous measures taken to insure emotional control and the availability and efficiency of rescue and medical facilities as well as social service and welfare organizations.

The two main ways recommended for insuring emotional control are: (1) preparatory education of the general public preceding the outbreak of atomic attacks and (2) on-the-spot communications from an authoritative source immediately following an atomic attack.

The results of the study presented in the book are of intrinsic academic interest; however, they are particularly valuable as substantiating evidence of the requirement for developing effective civil defense policies and for appraising the political, social, and moral consequences of atomic warfare.

Clinical Allergy: A Practical Guide to Diagnosis and Treatment. By Samuel J. Taub, M.D., F.A.C.P., Professor of Medicine and Chairman of Department of Allergic Diseases, Chicago Medical School, Chicago. Second edition. Cloth. $4.50. Pp. 276. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33d St., New York 16, 1951.

The second edition of this manual was written with the hope that "this handbook will continue to provide the general physician with a clear, simple, and accurate guide to effective diagnostic and therapeutic measures that he can readily apply in his own practice." There are no illustrations. The omission of a comprehensive bibliography is by design. The English composition is simple, clear, and easy to read. The author has practiced and has taught in the field of allergy successfully for many years. There are 13 chapters and an appendix. The appendix contains much practical information about sources of pollen, inhalant, ingestion, and contact allergens. There are useful diets and recipes. In general, the book accomplishes its purpose of presenting concise information about the field of allergy. It is doubtful if anyone could accomplish this to the satisfaction of a majority of experienced allergists.

The chapters on immunochemistry, dynamics of allergy, hayfever, colds, drug allergy, and serum sickness are more effective than the chapters on skin allergy, miscellaneous conditions, and parts of the chapters on asthma. The publisher has been remiss in permitting two sections on pathology to be printed in the chapter (pp. 90 and 99) on asthma. This plus redundancies and sketchy discussions of infectious asthma call for complete revision of the chapters on asthma. The two paragraphs on cortisone and the sentence on corticotropin ("Acthar") are inadequate. There is a table on page 205 with no legend or heading. The sentence at the top of page 206 has no connection with the preceding or succeeding material. An outline for cutaneous tests preliminary to the administration of antiserum is in the section on allergy from blood transfusion. The propriety of including a chapter on the preparation of extracts in a short clinical manual is debatable. In one reading of the book, the reviewer made 51 critical notations, most of them, however, relatively unimportant.

Whereas the manual contains a lot of practical information, simply presented, it does not fully meet the need for this type of book. There is much room for improvement; however, the same thing can be said for similar efforts by other authors. Allergy is a large subject. In spite of the criticisms mentioned in this review, the author's efforts to simplify it have, in general, been successful.

Practical Procedures in Clinical Medicine. By R. I. S. Bayliss, M.A., M.D., M.R.C.P., Medical Tutor and Senior Medical Registrar, Postgraduate Medical School of London, London. Cloth. 25s. Pp. 445, with 62 illustrations. J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London, W.1, 1950.

This volume is designed to provide senior students, house physicians, registrars, and general practitioners with descriptions of the laboratory and diagnostic procedures commonly used in studying patients. The first chapter describes, in detail, the types of syringes available for drawing blood, the size of needles to be used for subcutaneous and intravenous injections, and instructions on how to use a glass sliver from a broken microscope slide to prick the finger. The detail and arrangement is that of the usual nurses procedure book; diagnostic procedures and laboratory tests are grouped according to organ systems. Paracentesis is described in the chapter on disorders of the alimentary tract, and thoracentesis, in the chapter on disorders of the respiratory system. In addition to chapters on disorders of the alimentary tract, cardiovascular system, blood, liver, respiratory system, central nervous system, and endocrine glands, there are chapters on the indications for and technique of blood transfusion and on the place of radiology in clinical medicine. The last chapter combines such miscellaneous subjects as a table of atomic weight, diet tables, and a posologic table giving the average doses of over 400 drugs. Some of the drugs, such as Parrish's food (syrupus ferri phosphatias compositus), grey powder (mercury with chalk), and senna pods would only be of historic interest to physicians. The chapter also includes the average postmortem weights of organs, tables of weights and measures, and the method of performing vaccination.

The techniques of many common procedures, such as estimation of blood pressure, venesection, and digital examination of the rectum are described in great detail; the descriptions of other procedures, such as catheterization, lumbar puncture, and artificial pneumothorax are too sketchy to be of value to a novice. The more common tests used in the examination of blood and urine are described in the appropriate chapters, but with curious omissions. The technique for counting erythrocytes is given in detail, but there is no description of the cells as they are seen in a fixed smear. No formulas for reagents are supplied. The author

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The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

disclaims any intention of providing a text of clinical pathology, so that, for many tests, instructions are simply given to collect the specimen and send it to the laboratory. The paragraphs in each chapter on pathological physiology and the interpretation of analyses furnished by the clinical laboratory are too brief and in too general terms to provide a satisfactory basis for deciding when a particular test might be of value. This book is not of much value to either students or practitioners.

The Collected Papers of Adolf Meyer. Volume III: Medical Teaching. General editor, Eunice E. Winters. With introduction by Franklin G. Ebaugh, M.D., Professor of Psychiatry, the University of Colorado, Boulder and Denver. Cloth. $30 per set of 4 volumes. Pp. 577. Johns Hopkins Press, Homewood, Baltimore 18; Oxford University Press, Amen House, Warwick Sq., London, E.C.4, 1951.

These papers logically follow those on psychiatry (volume 2) in that they are mainly concerned with Meyer's psychiatric concepts and his methods of teaching. In these papers, Meyer develops the thesis that the patient should be considered as a whole, as a complex, integrated unit. In his teaching, he decried the method of choosing one complaint, one aspect of the patient's problem, and examining it from the viewpoint of any one particular system of psychiatry. The patient is a unit; the methods of approach should be unfettered, unlimited, and pluralistic. This type of thinking makes it easy to understand why Adolf Meyer placed little value on nosological psychiatry. His impatience with the rigidity of most systems of psychiatric classification was a prime mover in the establishment of his own more flexible system.

Dr. Meyer has served students of medicine and beginners in psychiatry well by the formulation of examination charts, life charts, and personality studies. The life charts, in their original form, are seldom used in present day psychiatry, but the examination tables still serve as models of orientation to most courses of psychiatry. The publication of this volume comes at an opportune moment, when psychiatric facilities are being extended and more attention is being focused on the teaching of psychiatry in the medical schools. Any teacher who is responsible for planning the curriculum of a medical school would profit by reading Meyer's essays. The volume ends with a series of biographical sketches by Dr. Meyer of the leading neurologists and psychiatrists of his day. Most of these men, such as Marie, von Monakow, Kraepelin, and Forel were pioneers in the teaching of psychiatry, and it is appropriate to include their brief biographies in a book devoted to medical teaching.

Daddy Was a Doctor. By Lorena Owens. Cloth. $2.75. Pp. 221, with illustrations by Paul Galdone. E. P. Dutton & Co., Inc., 286-302 Fourth Ave., New York 10, 1951.

Not only the hill country of southern Tennessee but nearly every other section of the country has the counterpart of "Doc" Peters, a 1905 graduate of a small school who knew the art of medicine better than the science, and who knew people better than anything else. This tale is a character sketch of Doc; his wife, mama; his mother, ma; and most of the patients found in a small town practice as seen through the eyes of a married daughter who comes home for the summer.

Although he was not the scientist a modern physician is expected to be, Doc knew his patients, hated hypochondriacs, and did a good job of mending the ills of his community. The humor is derived from the circumstances under which he worked, the partnership with Mama, and the way their patients expressed high regard for both of them. We have all known at least one Doc Peters. It is nice to have this tribute to a passing generation of simple persons who led complex lives.

Vertebrate Sexual Cycles. By W. S. Bullough, D.Sc., Sorby Research Fellow of Royal Society of London. Cloth. $1.50. Pp. 117, with 12 illustrations. John Wiley & Sons, Inc., 440 Fourth Ave., New York 16; Methuen & Co., Ltd., 36 Essex St., Strand, London, W.C.2, 1951.

This little volume is a brief but well-worded résumé of current information on the sexual cycles and breeding habits of vertebrates. Although its broad coverage is designed to appeal to the zoologist rather than to the medical man, the book contains much interesting factual information in an easily assimilable form.

The Changing Years: What to Do about the Menopause. By Madeline Gray. Cloth. $2.75. Pp. 224. Doubleday & Company, Inc., Garden City, New York, 1951.

The author has presented the problems of the menopausal woman in a clear and sympathetic manner. She has gathered information from a number of reliable sources and presented it in simple straightforward language, which is easy to understand.

The relationship of the ductless glands to the phenomena of puberty, menstruation, and menopause is clarified, and many superstitions are explained and discounted. The relationship between the patient and physician is stressed, and the help women can get from medical treatment and the means by which they must help themselves is outlined. Many of the vague fears regarding mental disease, cancer, high blood pressure, and arthritis are shown to be groundless. The symptoms of the menopause and their transitory nature are pointed out. Hormone treatment is outlined and the origin and action of hormones considered. The conflict between the well-bred woman's early training in regard to sex and what is normally experienced in married life and some mistaken ideas about views of the church in these matters are explored, and quotations from important clerical persons are presented. The importance of the preservation of a trim figure and the ability to do so are pointed out, and specific dietary instruction is included. A chapter on the changes in the male sex life is included, and the similarity of the problems of the two sexes as well as their differences is well presented.

The book is well written and informative and should be useful as a lay educational medium in this field.

The Practice of Endocrinology. Edited by Raymond Greene, M.A., D.M., M.R.C.P. Second edition. Cloth. $12.50. Pp. 389, with 81 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Eyre & Spottiswoode, Ltd., 14-16 Bedford St., Strand, London, W.C.2, 1951.

This is an American reprint of a popular British text that originally appeared under the authorship of six prominent endocrinologists and the editor of the present edition, who has undertaken the entire revision of this second edition. This reduction in the number of authors has resulted in greater unity, which is always difficult to attain with multiple authorship. The book is intended for the general practitioner, and, for this reason, the theoretical sections in the earlier edition have been deleted in favor of new matter of purely practical interest. The result is a concise, well-written outline of clinical endocrinology. The subject is well covered; the style is clear and succinct; the illustrations are excellent; and the opinions expressed are sound and up-to-date. Despite some criticisms, such as the omission of mentioning the use of cortisone in the treatment of Addison's disease, the failure to mention the Sulkowitz reagent in regulating the dosage of dihydrotachysterol in hypoparathyroidism, and an occasional statement to which exception may be taken, this book can be recommended as a desirable addition to the library of the general practitioner.

Treatment by Manipulation. By H. Jackson Burrows, M.D., F.R.C.S., F.R.A.C.S., Orthopædic Surgeon, St. Bartholomew's Hospital, London, and W. D. Coltart, M.B., F.R.C.S., Assistant Orthopædic Surgeon, St. Bartholomew's Hospital. Second edition. Cloth. 12s. 6d. Pp. 80, with 29 illustrations. Published on behalf of "Practitioner" 5 Bentinck St., London, W.1, by Eyre & Spottiswoode, 15 Bedford St., Strand, London, W.C.2, 1951.

This book deals chiefly with the manipulative treatment of chronic sprain and strain. It is stated that "Many members of the medical profession know too little of the selection of cases for manipulation, its technique and results which may be expected from it." This monograph concerns itself with practical and elementary matters rather than a detailed and hypothetical consideration of the subject. The book contains headings such as the "Selection of Cases for Manipulation" and "The General Management of Manipulation Cases." It is indicated that, for this type of manipulation, anesthesia is invariably used. The dangers and failures of manipulation are discussed. Afflictions of individual parts of the body and their manipulation are then discussed; good illustrations that show the techniques described in the text are included. This book will be of great interest to the orthopedic surgeon.

Studies of Undernutrition, Wuppertal 1946-9. By members of Department of Experimental Medicine, Cambridge, and associated workers. Medical Research Council Special Report Series no. 275. Paper. 12s. 6d. Pp. 465, with illustrations. His Majesty's Stationery Office, P. O. Box 569, London, S.E.1, 1951.

This volume was written by the members of the Department of Experimental Medicine at Cambridge, England, and associated workers, who had the opportunity to study human nutrition from the summer of 1946 to the latter part of 1948. The base of their work was the laboratories and hospitals at Wuppertal, a community of over half a million persons, just south of the Ruhr, in Germany. The leader of the team was Dr. R. A. McCance, who was assisted by Dr. E. M. Widdowson. The book is divided into 29 chapters, and covers many of the technical problems of nutritional difficulties that have been seen in recent years in wartorn countries. The volume is distinguished by the exceptional coverage of the historical literature in this field and is valuable because of the documentation. The discussions of the physical findings, chemical laboratory work, and the conclusions based on them are conservative, as would be expected from this authorship; for example, the discussion of hunger edema recognizes the protein, vitamin, and mineral factors, the anatomic and dynamic features of importance, the influences exerted by several endocrine activities, and the rational relationship of several of these forces to each other.

In considering some of the disturbances of the nervous system, it is striking that although the evidence suggests frequent and significant reduction in circulating calcium in the blood, the authors do not conclude that this is a factor in the exaggerated reflex responses. There is a tendency to attribute this reflex response to emotional disturbances, which are obviously a significant part of the historic background of the persons studied. In searching for new and more satisfactory objective evidence of nutritional status, the authors gave much attention to the study of serum cholinesterase. They include some results of experimental work with animals, and are inclined to think this a useful technique, although they do not think it indicative of any particular type of malnutrition. There is interesting evidence of decalcification of the skeleton, although the roentgenographic evidence is not as impressive as the chemical studies. A fascinating fraction of the study is the series of observations on the response to unlimited food of persons who had been deprived for a long time. Physical, chemical, and psychological responses are discussed, and additional light is thrown on the nature of the nutritional deficits that have incurred. In addition to a number of line drawings, the appendix includes 62 interesting plates that illustrate the features of the volume. This work is an important item in any library that endeavors to have the original data and recent comments on human malnutrition.

Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association, with the Comments That Have Appeared in The Journal of the American Medical Association. Cloth. $2. Pp. 106. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1950.

The report of the 1949 annual meeting of the Council, included in this reprint, outlines the initiatory steps that eventuated in some of the other reports appearing in this small but valuable reprint. It may be safely assumed that other deliberations detailed in this particular report will result in the considered and definitive action for which the Council is noted. Perusal of this report as well as of the entire reprint is recommended, especially to those who are not familiar with the Council's valuable work and the increasing emphasis given, in recent years, to forward looking action on the frontiers of medical progress.

The work of two of the Council's special committees is the subject of two important reports: that of the Committee on Research, dealing with cancer and steroid hormone therapy in mammary cancer metastatic to bone, and that of the newer Committee on Pesticides, dealing with the pharmacology and toxicology of certain organic phosphorus insecticides. The first study is a continuation of work begun by the Committee in 1949; this study, which will be continued, has already resulted in valuable clarification of our knowledge of cancer. The second study represents the start of an organized and definitive text on pesticides; this should be an important contribution to the field of preventive medicine.

In the report on the status of BCG vaccine, it is concluded that further studies are needed before general use of this agent in the United States can be recommended. The report on chemotherapy of tuberculosis, third in a series representing cooperative study of this subject with the Veterans Administration and the Navy, covers 7,000 patients treated by 22 surgeons, using streptomycin and dihydrostreptomycin. It concludes by emphasizing the importance of surgical procedures in connection with chemotherapy, calling attention to the reduction of toxic manifestations by the use of a 1 gm. (or less) daily dose and noting the delayed development of resistant microorganisms by concurrent administration of *p*-aminobenzoate.

Two other status reports are on antihistaminics in the treatment of colds and on adrenal and pituitary hormones in the treatment of arthritis and other diseases. The first report analyzes the work of investigators on 2,357 cases, points out that available data are only suggestive of beneficial effects, and outlines a technique for further investigation. The report on adrenal and pituitary hormones, cortisone and corticotropin (ACTH), gives the essentials of the history and composition of these agents, points out that improvement lasts only as long as they are administered, and emphasizes the danger of their continued use and "rebound" on discontinuance. The reprint also contains reports on routine Council actions.

Epileptic Seizure Patterns: A Study of the Localizing Value of Initial Phenomena in Focal Cortical Seizures. By Wilder Penfield, C.M.G., M.D., D.Sc., Professor of Neurology and Neurosurgery, McGill University, Montreal, and Kristian Kristiansen, M.D., Assistant Surgeon, in charge Neurosurgery, Oslo City Hospital, Oslo, Norway. Cloth. $3. Pp. 104, with 18 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1951.

Where in the brain do the seizures of epilepsy originate? This question is of profound importance to students of the brain and to clinicians who wish to understand and treat epilepsy. The authors have analyzed data from 259 patients having focal seizures. In 222 of these, the point of origin was identified either by reproduction of the initial phenomenon by cortical stimulation by electroencephalographic recordings from the cortex or by observed abnormality at operation (usually atrophy or scars) of the cortex. The information derived relates to the superficial layer of the brain only; it is succinctly presented in a well-printed monograph. There are 18 drawings in which the location of the initial symptom of each patient is represented by a circle on the cerebrum. There are 33 references. The size of the book is no measure of the many thousands of hours that must have been spent in meticulous study of these patients. Initial seizure symptoms include unconsciousness and motor, sensory, autonomic, psychical, and miscellaneous phenomena. For a detailed description of techniques and case reports, the reader will need to consult previous books and articles by the principal author and his various associates. In the concluding chapter on clinical application, the authors limit the word epilepsy to cases "in which no brain lesion or cortical focus can be demonstrated," and in which "the electroencephalogram demonstrates bilateral three per second synchronous waves." This would seem to be too narrow a restriction; in fact, the subject of classification and terminology requires more than a few pages and discussions of concepts of epilepsy should embrace more than the areas of origin.

Speech Training: A Handbook for Students. By A. Musgrave Horner. Cloth. $3.75. Pp. 176, with 8 illustrations. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1951.

The author of this book is a lecturer on speech training at Stranmillis College, Belfast. The book, intended mainly for teachers and students, provides material for practice and demonstration in speech training. Although it does not seem to be written for the speech therapist who handles patients such as those afflicted with cerebral palsy, the book does contain many practical points that may be used in speech training.

QUERIES AND MINOR NOTES

REMOVAL OF A NORMAL APPENDIX

TO THE EDITOR:—*A difference of opinion exists among the physicians of this hospital concerning criteria to be used in determining whether an appendectomy should be performed during a laparotomy or a cesarean section for ectopic pregnancy. Some think that the appendectomy could be performed during such a time with no danger or adverse side-effects; others believe that an appendectomy should not be performed under those circumstances. Can you supply information on this question?* *M.D., Venezuela.*

ANSWER.—The routine removal of a normal appendix at laparotomy is not advisable. Regardless of the care with which the appendix is removed, the procedure increases the hazard of the operation and may increase the likelihood of postoperative complications. Simple operative procedures performed on young persons, such as oophorocystectomy, may include appendectomy without increased risk. An abnormal or adherent appendix should be removed if the procedure will not unduly complicate the patient's recovery.

Removal of the appendix at cesarean section is unwarranted. Abdominal delivery may be accompanied by considerable blood loss and extensive soiling of the peritoneal cavity by amniotic fluid and its contents. To invade the gastrointestinal tract, even with great care, is to add to the danger of infection. Present reliance on miraculous antibiotic drugs must not be allowed to diminish the importance of following sound surgical principles developed in years of clinical experience.

RETINITIS PIGMENTOSA

TO THE EDITOR:—*(1) What is the prognosis for retinitis pigmentosa in a 7-year-old boy? The Wassermann test reactions for himself and both his parents are negative. So far, no narrowing of the retinal arteries can be seen. No one else in his family has, or has had, this disease. (2) What is the consensus among ophthalmologists in America on the value of treatment by means of subconjunctival implantation of placental tissue done at six month intervals? I am told that this treatment is now widely used in European countries. The boy is already being given vitamin A, and his parents have been warned to watch for signs of vitamin A overdosage.*

M.D., India.

ANSWER.—1. According to Fralick (Symposium: Primary Chorioretinal Aberrations with Night Blindness: Treatment and Conclusions, *Tr. Am. Acad. Ophth.* **54:**662, 1950), there are no available statistics showing what percentage of persons with this disease actually become blind. The earlier in life the disease becomes manifest, the more serious is the prognosis, generally; however, the progress of the disease is slow, and few persons completely lose all vision. 2. Subconjunctival implantation of placental tissue has never been widely used in this country. Gordon (Experimental Treatment of Retinitis Pigmentosa, *Tr. Am. Acad. Ophth.* **52:**191, 1948) used a variety of biogenic stimulators in the treatment of retinitis pigmentosa and found them to be without value. Saltzman and Haig (Treatment of Retinitis Pigmentosa with Cod Liver Oil Injections and Placental Implantation, *Arch. Ophth.* **43:**419, 1950) treated 27 patients with cod liver oil injections and subcutaneous implantation of preserved placenta. In no case was there a significant increase in visual acuity or in the scope of the visual field, and although a few patients showed subjective improvement, this was not confirmed by careful study.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

BIBLICAL HYSSOP AND PENICILLIN

TO THE EDITOR:—*Does the hyssop referred to in Psalm 51 "Purge me with hyssop, and I shall be clean: wash me, and I shall be whiter than snow," contain any penicillin?*

V. G. Logan, M.D., American Falls, Idaho.

This inquiry was referred to two consultants, whose respective replies follow.—ED.

ANSWER.—The hyssop mentioned in Psalm 51, verse 9, contains no penicillin and is not related to any fungus from which penicillin-like substances can be obtained. The impression that hyssop has something to do with penicillin is a misapprehension caused by curious philological and semantological circumstances. The Latin translation of the Bible, the Vulgate, reads as follows: "Asperges me hyssopo et mundabar" (Purge me with hyssop and I shall be clean). The Latin verb *aspergere*, means to sprinkle or scatter. It is the same word from which our English "aspersion" is derived. In Roman Catholic churches the sprinkling of holy water was performed by dipping into the water a round brush, to which the name of aspergill or aspergillum was given. The hyssop of the Bible was employed for a purely ritual purification involving the dipping of a bunch of hyssop in blood or water and sprinkling it. It happens that two of the commonest molds studied by mycologists are of the genus Aspergillus, a mold, the conidiophores of which resemble a round brush, and of the genus Penicillium, the conidiophores of which look like a tufted or pencil brush. It was therefore argued that, inasmuch as sprinkling with hyssop produced ritual cleansing, and inasmuch as the above molds are sources of valuable antibiotics, the hyssop and the molds were related not only in the ritual sense of the words but also in respect to their antibiotic or antibacterial properties. It is interesting that several species of the mold family Aspergillus have yielded penicillin-like chemicals. For instance, Adler and Wintersteiner published a paper entitled "A Reinvestigation of Flavacin, the Penicillin Produced by Aspergillus Flavus" (*J. Biol. Chem.* **176:**873, 1948). Penicillin-like chemicals have been found also in Aspergillus parasiticus and Aspergillus giganteus.

ANSWER.—A careful survey of the Old Testament, together with a perusal of the literature on botanicals, especially that of the time when the St. James version was written, does not reveal any evidence that hyssop (Hyssopus officinalis) has antibiotic properties. The continental variety of hyssop, known as Gratiola officinalis, was the species used in herbal medicine in Europe. It has a bitter, nauseating taste, and acts as a purgative, emetic, and diuretic when taken internally. In herbal medicine it was used for the treatment of dropsy among other diseases.

The hyssop that is frequently mentioned in the Scriptures (Exod. XIII: 22; Lev. XIV: 4, 6; Num. XIX: 6, 18; I Kings V: 13; Ps. LI: 9) was not Hyssopus officinalis. There is much dispute about just what herb was meant, but it would seem from the writings of Maimonides and others that the herb referred to was a variety of wild thyme that grows abundantly in Syria and Palestine and has similar medicinal properties to H. officinalis.

WATER SOFTENERS

TO THE EDITOR:—*Is the addition of sodium chloride required in the manufacture of all varieties of water softeners? What chemical changes occur in softening water for domestic purposes? Is this softened water injurious to healthy persons when used for drinking purposes?* *M.D., Texas.*

ANSWER.—Sodium chloride is scarcely involved in common methods of water softening, either the lime-soda ash or zeolite processes. Some confusion has occurred because heavy brines are used in the rejuvenation of zeolite beds, but these do not enter the potable water. In the lime-soda ash procedure calcium hydroxide and sodium carbonate act on soluble compounds of

calcium and magnesium, converting them to insoluble forms that are removed by filtration and settling. The lime alone is sometimes sufficient. If soda ash is added, small quantities of sodium chloride may form and remain in the potable water. The zeolites are double silicates of aluminum and iron with sodium bases; through their action, an exchange takes place with the unwanted calcium and magnesium. In both processes, the sodium appears chiefly as the sulfate. Many natural waters contain much more sodium chloride than that produced in water softening. If the medical demand is for wholly salt-free water, then distilled water should be used in place of either natural or softened water.

GASTRIC HEMORRHAGE, EDEMA, AND CHLOROPHYLL

To the Editor:—*Is giving chlorophyll to counteract a repulsive odor contraindicated when gastric ulcers or hyperchlorhydria are evident? I have been giving it to a Negro man, who has edema that is so acute that a large necrotic area has sloughed out from the left leg. He has had two massive gastric hemorrhages and a history of gastric ulcer. At present, he has a slight hyperchlorhydria. What factor other than chlorophyll might be the cause of these massive hemorrhages?*

DeWitt S. Lowe, M.D., Hiawatha, Kan.

Answer.—There is probably no contraindication for the use of chlorophyll as a deodorant in this particular instance. Chlorophyll is generally considered to be nonirritating and is supposed to aid in the healing of skin wounds and ulcers by stimulating the production of normal granulation tissue. In fact, chlorophyll has been combined with aluminum hydroxide and magnesium trisilicate in an okra base for the treatment of peptic ulcer. The rationale for chlorophyll in this mixture is presumably to aid in tissue repair.

The etiology of the large necrotic area that has sloughed out from the left leg may have no relation to the hemorrhages from the stomach. There probably are two independent conditions, one, a lesion of the leg, and the other, hemorrhage from an upper gastrointestinal lesion. Roentgen studies should be made when the patient has stopped hemorrhaging from the stomach to determine whether a gastric lesion is present. It is difficult to determine the etiology of the lesion of the leg from the information given. It is assumed that the edema and ulceration is unilateral. It is possible that this person has a sickle cell anemia, with an associated gastric hemorrhage. Such conditions as a localized syphilitic ulcer, an ulcer associated with varicosities, and ulceration due to neoplasm or infection must be considered. It is advisable for the physician to have a roentgenogram taken of the leg in order to rule out the possibility of an osteomyelitis with suppuration and associated soft tissue ulceration. Finally, a retroperitoneal or abdominal mass, with involvement of the venous return from the lower extremities, should be considered.

TREATMENT OF ANGIONEUROTIC EDEMA

To the Editor:—*A patient with urticaria responded well to food restriction, local therapy, and antihistamines. A short time later, an angioneurotic edema developed on one thigh and has remained unchanged; occasionally, it is painful. At first, some relief was afforded by rest, cold compresses and two tablets of "phenergan" (a new synthetic antihistaminic derived from phenothiazine) at night. A colleague has advised using a combination of rutin, 60 mg. and cevitamic acid, 300 mg., twice a day. Is this advisable?* *M.D., New Jersey.*

Answer.—It is not likely that the combination of rutin and cevitamic acid will be of much value, but, in lieu of any better therapeutic suggestions, it is worth a trial. If this is not beneficial, procaine or an antihistaminic, administered intravenously, might be tried. It is suggested that careful attention be given to the wearing apparel and habits of the patient that might produce minor pressure at the site where the angioneurotic edema develops. There is evidence that after urticaria, there is a "lability" of the vessels, so that at areas of minor pressure or trauma there will be exudation.

GREEN DISCHARGE FROM BREAST

To the Editor:—*A 26-year-old white woman complains that she has been able to express fluid, about the color of dark green ink but a little thicker, from her left breast, for the past six months. For several years, she has been able to express a milky substance from her breast, but she has noted no tenderness or lumps in either breast. The patient is married, but she has not been able to become pregnant. Menstrual periods began at the age of 12 and have always been regular, about 28 days apart, and of 5 days' duration. Until the age of 19, she had cramps during her periods. At that time, a uterine suspension was done. Since then, she has had no dysmenorrhea. There is usually tenderness of the breasts during her periods. Physical examination, at present, shows normal results, with the exception of the dark green fluid that is expressed from the left breast when pressure is applied in the upper inner quadrant. There is a milky substance expressed at the same time. The breast is not tender, and masses are not palpable. The patient is not uncomfortable and has no pain from this complaint; however, she was afraid that she had cancer. Please suggest diagnosis and treatment.*

Lloyd L. Long Jr., M.D., Ardmore, Okla.

Answer.—It is not unusual for fluid of various colors to be spontaneously or artificially expressed from the nipples, and it is not unusual for this fluid to have a green hue. It usually signifies intraductal hyperplasia and/or papillomatosis, and it is often associated with so-called chronic cystic mastitis. There is no direct relationship between this type of discharge and cancer of the breast, although the two may exist coincidentally. Only when the discharge has a sanguineous character need there be concern. When a bloody discharge is present, malignant intraductal papilloma must be considered, even though no mass is palpable in the breast. Treatment consists of periodic observation to guard against the development of breast disease that would require more active therapy.

NITRIC ACID FUMES AND NITROGEN DIOXIDE GAS

To the Editor:—*What hazards accompany the presence of nitric acid fumes and nitrogen dioxide gas in the atmosphere of a factory? What concentration of the gases (parts per million) is safe for the workers? How would the length of exposure affect them? What should be the period of exposure in the contaminated room and the length of the rest period between exposures? How can a patient be tested for excessive exposure? What criteria must be used to determine whether an employee may continue to work in a contaminated environment?* *Herbert Berger, M.D., Staten Island, N. Y.*

Answer.—For present purposes, disregarding the surface action of nitric acid, these two substances may be considered as one. The upper limit of concentration for sustained exposure is now widely accepted as 25 ppm. When the concentration is above 100 ppm, even exposure for a short time, such as for one hour, is dangerous. Lower concentrations such as 50 to 75 ppm may lead to noticeable throat irritation. Control of the concentration is far more important than timing the workers' exposure to an uncertain concentration. This is true despite the fact that laboratory determination of these gases is not easy. In exposure to a constant concentration, the quantity reaching the lungs of any one worker is limited to the volume of tidal air. It is often true that toward the end of a long period of hard work done in the presence of high temperatures, the intake of air, including any contaminant, may be double that for the first hour of the work day, when conditions are more favorable. Although exposure may result in systemic disease, the primary threat is respiratory tract edema, which often is delayed and is unpredictable except when considered in relation to the concentration levels of these gases. As a rule, throat irritation or coughing not readily accounted for should serve as a warning. Overexertion is undesirable during exposure to nitrogen gases and is exceedingly damaging after significant exposure has occurred. Eventually, nitrites may be formed within the body, and their presence may be manifested as low blood pressure, dizziness, headache, and methemoglobinemia. Such manifestations constitute warnings but provide no guide to the possibility of pulmo-

nary tract edema, which may be antecedent. The objective should be to maintain exposure below damaging levels. The workers may evince no signs of overexposure prior to those indicating severe damage.

TOXICITY OF PAINT SOLVENTS

To the Editor:—*A patient, after working in a factory paint room for three or four days, on four different occasions has had abdominal cramps in the area of the navel and has had vomiting attacks that disappear after 24 hours. His job is to apply a lead-free varnish to tractors. Please discuss this condition.* *R. G. Stoll, M.D., Chickasha, Okla.*

Answer.—The information furnished is inadequate for an exact reply. Some solvents, when inhaled, do provoke gastric disturbances. This is notably true of some chlorinated hydrocarbons, but these compounds are not usually present in common paint coatings. Even naphtha is known to possess this property, but possibly it affects only overly susceptible persons. At times, the disturbance produced simulates an allergic response, since, on occasion, trivial exposure is sufficient to excite immediate response. The combustion products from motor vehicles burning hydrocarbons often cause minor gastric upsets, but, in these cases, aldehydes are more likely to be the cause. The presence of chlorinated hydrocarbons may be detected with an halide lamp. If the test proves strongly positive, their source and type should be determined.

FUMES FROM THE GALVANIZING PROCESS

To the Editor:—*Would the fumes from a galvanizing process involving zinc and copper cause stippling of the red blood cells in a patient exposed to them?* *M.D., Massachusetts.*

Answer.—Ordinarily, zinc, iron, and copper (if actually present) do not significantly provoke stippling. Up to 1.5% of red blood cells of healthy adults contain demonstrable basophilic substance not regularly in the stipple form. If, in the present instance, stippling is outstanding and is unaccounted for by anemia unrelated to work, suspect lead intoxication, since lead is an ubiquitous impurity in commercial metals and alloys. It may be detected in the workroom atmosphere or in the urine of the patient (in quantities above normal). In addition, the patient should be examined for clinical indications of lead intoxication.

POSITIVE WASSERMANN FOLLOWING SMALLPOX VACCINATION

To the Editor:—*Can a smallpox vaccination produce a positive Wassermann reaction? The vaccination was given two weeks before the Wassermann test was taken. The reaction to the vaccination was 3+.* *M.D., Texas.*

Answer.—There are ample observations showing that all tests for syphilis, whether complement fixation or precipitation, will in certain vaccinated persons call forth positive serologic reactions. Generally, positivity begins about two weeks following vaccination and lasts for two or three months. An extensive discussion of false positive reactions resulting from smallpox vaccination, as well as from other causes, is presented by Herman Beerman, in "Biologic False Positive Reactions to Tests for Syphilis." (*Am. J. M. Sc.* **209:**525-542 [April] and **210:**524-548 [Oct.] 1945.)

DIARRHEA FOLLOWING COITUS

To the Editor:—*A healthy young married man develops acute diarrhea the day following coitus. There is mucus in the stool, but no blood, and he may have a normal stool on the same day, prior to the loose one. The condition has been alleviated by antispasmodic therapy and sedation. He has no emotional conflict that I can discover. Results of physical examination are normal. What drug would be most appropriate for this condition?* *Orin Q. Flint, M.D., Delhi, N. Y.*

Answer.—The occurrence of acute diarrhea in a healthy young married man on the day following coitus is not rare. It is dependent on several factors. First, diarrhea of this type is usually psychogenic. Second, since the energy expended may lead to hypoglycemia, diarrhea is most likely to occur before breakfast. Ingestion of food in the evening should prevent this manifestation. The only drugs that are appropriate are those he has already received; any parasympatholytic drug, plus a sedative, such as phenobarbital sodium, is sufficient. It may be wise for this person to consult a psychiatrist, who can determine the existence of an emotional disturbance. Such a disturbance can cause an increase in the peristalsis of the small and large bowel.

CYSTITIS FOLLOWING INTERCOURSE

To the Editor:—*The query entitled "Cystitis Following Intercourse" in* The Journal (**146:**1546 [Aug. 18] 1951) *was not completely answered by the consultant or by the subsequent correspondence in* The Journal (**147:**1720 [Dec. 22] 1951). *The history was that of a woman in whom cystitis repeatedly developed (controllable with antibiotics) one to three days after intercourse from the beginning of her marriage. To make a diagnosis of cystitis, pyuria was presumably demonstrated; the further successful therapy by antibiotics should completely rule out a psychosomatic diagnosis, or "some disease of the gastrointestinal tract." Previous answers suggested cystoscopic examination, x-ray examinations, intravenous pyelogram, urethroscopy, and panendoscopy, presumably in an effort to locate a chronic source. Certainly, the periurethral glands are a possibility as the site of a chronic infection, which could flare up as a urethritis or cystitis following intercourse but a more likely source of infection has been overlooked—the male partner.*

The onset of this recurring cystitis was at the beginning of her marriage. Ordinarily a resistance to the organisms causing "honeymoon cystitis" is developed, but this does not always occur especially if the infection is prematurely terminated by antibiotics. The husband's genitals, which carry a large variety of micro-organisms, may serve as a constant source of reinfection to his partner. These organisms may come from any chronic genital infection, such as prostatitis or urethritis, or they may be carried asymptomatically beneath the prepuce. The part played by the male has long been recognized in some types of cervicitis and vaginitis.

In correction of the problem presented, I would suggest that: 1. Both husband and wife should be examined, with inspection of the urethra, using sounds if needed to determine the presence of strictures or periurethritis, examination of prostatic fluid, and examination of the vagina and cervix. Any chronic infection found and eliminated will probably terminate the condition. 2. If no chronic infection is found, the husband should be advised to wash his genitals thoroughly with soap and water before each coitus, with emphasis on cleaning beneath the prepuce. 3. Only if the above two steps have proved unrewarding would one feel justified in proceeding to more intensive diagnostic search, such as urethroscopy, cystoscopy, and pyelograms, which should involve the husband as well as the wife. *Dr. Victor E. Archer*
10312 Insley St., Silver Spring, Md.

NOSE DROPS

To the Editor:—*In the answer to the question about nose drops in Queries and Minor Notes, Jan. 5, 1952, the consultant left out one of the most important conditions for the use of nasal vasoconstrictors, namely, early closure of the eustachian tube due to upper respiratory infection. Potent vasoconstrictors, such as epinephrine, ephedrine, and phenylephrine (neo-synephrine®), are effective in shrinking the swollen and inflamed mucous membrane of the tympanopharyngeal (eustachian) tube, thus restoring normal patency, ventilation, and drainage.*

Instead of using the so-called ear drops, which have no effect at all when dropped into the external auditory canal with an intact drum, it is more logical to use nasal vasoconstrictors and thus reach the tympani easily via the natural route. The early judicious use of nasal vasoconstrictors in pre-penicillin days has prevented many a middle ear and mastoid suppuration. *Joseph W. Miller, M.D.*
431 N. E. 30th St.
Miami, Fla.

JOURNALS ABSTRACTED IN THE CURRENT MEDICAL LITERATURE DEPARTMENT, JANUARY-APRIL 1952

Titles have been listed or abstracts made of important articles in the following journals in the Current Literature Department of THE JOURNAL during the past four months. Any of the journals, except those starred, will be lent by THE JOURNAL to individual subscribers in Continental United States and Canada and to members of the American Medical Association and its student organization. No charge is made to members, but the fee for other borrowers is 15 cents in stamps for each periodical. Three journals may be borrowed at a time for a period not exceeding five days. Requests should be addressed to the Library of the American Medical Association. Thus most of these journals are accessible to the general practitioner.

*A. M. A. American Journal of Diseases of Children. Chicago.
*A. M. A. Archives of Dermatology and Syphilology. Chicago
*A. M. A. Archives of Industrial Hygiene and Occupational Medicine. Chicago.
*A. M. A. Archives of Internal Medicine. Chicago.
*A. M. A. Archives of Neurology and Psychiatry. Chicago.
*A. M. A. Archives of Ophthalmology. Chicago.
*A. M. A. Archives of Otolaryngology. Chicago.
*A. M. A. Archives of Pathology. Chicago.
*A. M. A. Archives of Surgery. Chicago.
Acta chirurgica belgica. Brussels.
Acta chirurgica scandinavica. Stockholm.
Acta endocrinologica. Copenhagen.
Acta endocrinologica iberica. Porto.
Acta haematologica. Basel.
Acta medica scandinavica. Stockholm.
Acta obstetricia et gynecologica scandinavica. Stockholm.
Acta tuberculosea belgica. Brussels.
American Heart Journal. St. Louis.
American Journal of Clinical Pathology. Baltimore.
American Journal of Digestive Diseases. Fort Wayne, Ind.
American Journal of Hygiene. Baltimore.
American Journal of the Medical Sciences. Philadelphia.
American Journal of Medicine. New York.
American Journal of Obstetrics and Gynecology. St. Louis.
American Journal of Ophthalmology. Chicago.
American Journal of Orthopsychiatry. New York.
American Journal of Pathology. Ann Arbor, Mich.
American Journal of Physiology. Baltimore.
American Journal of Proctology. New York.
American Journal of Psychiatry. New York.
American Journal of Psychotherapy. New York.
American Journal of Public Health. New York.
American Journal of Roentgenol. and Radium Therapy. Springfield, Ill.
American Journal of Surgery. New York.
American Journal of Syphilis, Gonor. and Venereal Diseases. St. Louis.
American Journal of Tropical Medicine. Baltimore.
American Practitioner and Digest of Treatment. Philadelphia.
American Review of Tuberculosis. New York.
American Surgeon. Atlanta, Ga.
Anesthesiology. New York.
Angiology. Baltimore.
Annales chirurgiae et gynaecologiae Fenniae. Helsinki.
Annales medicinae internae Fenniae. Helsinki.
Annales paediatrici. Basel.
Annals of Allergy. Minneapolis.
Annals of Internal Medicine. Lancaster, Pa.
Annals of Otology, Rhinology and Laryngology. St. Louis.
Annals of the Rheumatic Diseases. London.
Annals of Surgery. Philadelphia.
Annals of Western Medicine and Surgery. Los Angeles.
Antibiotics and Chemotherapy. Washington, D. C.
Archiv für Kinderheilkunde. Stuttgart.
Archiv für klinische Chirurgie. Heidelberg.
Archives of Disease in Childhood. London.
Archives des maladies du coeur et des vaisseaux. Paris.
Archives of Pediatrics. New York.
Archives of Physical Medicine. Chicago.
Archivos uruguayos de medicina, cirugía y especialidades. Montevideo.
Archivum chirurgicum neerlandicum. Arnhem.
Arizona Medicine. Phoenix.
Arquivos brasileiros de cardiologia. São Paulo.
Arquivos de neuro-psiquiatria. São Paulo.
Australian and New Zealand Journal of Surgery. Sydney.
Bacteriological Reviews. Baltimore.
Beiträge zur Klinik der Tuberkulose. Berlin-Heidelberg.
Beiträge zur klinischen Chirurgie. Berlin.
Biochemical Journal. London.
Blood. New York.
Boletín de la Sociedad chilena de obstetricia y ginecologia. Santiago.
Brain. London.
Brasil-médico. Rio de Janeiro.
British Heart Journal. London.
British Journal of Cancer. London.
British Journal of Dermatology. London.
British Journal of Experimental Pathology. London.
British Journal of Industrial Medicine. London.
British Journal of Nutrition. London.
British Journal of Ophthalmology. London.
British Journal of Plastic Surgery. Edinburgh.
British Journal of Radiology. London.
British Journal of Surgery. Bristol.
British Journal of Tuberculosis. London.
British Journal of Urology. London.
British Journal of Venereal Diseases. London.
British Medical Journal. London.
Bruxelles-médical. Brussels.
Bulletin of the Johns Hopkins Hospital. Baltimore.
Bulletin of the New York Academy of Medicine. New York.
Bullettino delle scienze mediche. Bologna.
California Medicine. San Francisco.
Canadian Journal of Medical Sciences. Ottawa.
Canadian Journal of Public Health. Toronto.
Canadian Medical Association Journal. Montreal.
Cancer. Philadelphia.
Cancer Research. Chicago.
Cardiologia. Basel.
Chirurg. Berlin-Heidelberg.
Cincinnati Journal of Medicine. Cincinnati.
Circulation. New York.
Clínica pediatrica. Bologna.
Clínica tisiológica. Rio de Janeiro.
Clinical Science. London.
Connecticut State Medical Journal. Hartford.
Delaware State Medical Journal. Wilmington.
Deutsche medizinische Wochenschrift. Stuttgart.
Deutsche Zeitschrift für Nervenheilkunde. Heidelberg.
Diseases of Chest. Chicago.
Documenta neerlandica et indonesica de morbis tropicis. Amsterdam.
East African Medical Journal. Nairobi.
Edinburgh Medical Journal. Edinburgh.
Electroencephalography and Clinical Neurophysiology. Boston.
Endocrinology. Springfield, Ill.
Eye, Ear, Nose and Throat Monthly. Chicago.
Fortschritte auf dem Gebiete der Röntgenstrahlen vereinigt mit Röntgenpraxis. Stuttgart.
Gastroenterology. Baltimore.
Geburtshilfe und Frauenheilkunde. Stuttgart.
Geriatrics. Minneapolis.
Glasgow Medical Journal. Glasgow.
GP (Journal of American Academy of General Practice). Kansas City, Mo.
Hawaii Medical Journal. Honolulu.
Hoja tisiológica. Montevideo.
Hospital. Rio de Janeiro.
Illinois Medical Journal. Chicago.
Industrial Medicine and Surgery. Chicago.
International Journal of Leprosy. New Orleans.
Irish Journal of Medical Science. Dublin.
Journal of Allergy. St. Louis.
Journal of American Medical Women's Association. Nashville, Tenn.
Journal of Applied Physiology. Washington, D. C.
Journal of Arkansas Medical Society. Fort Smith.
Journal of Aviation Medicine. St. Paul.
Journal of Bacteriology. Baltimore.
Journal of Bone and Joint Surgery. Boston.
Journal of Clinical Endocrinology. Springfield, Ill.
Journal of Clinical Investigation. Cincinnati.
Journal of Clinical Pathology. London.
Journal of Endocrinology. London.
Journal of Experimental Medicine. New York.
Journal of the Florida Medical Association. Jacksonville.
Journal français de médecine et chirurgie thoraciques. Paris.
Journal of Gerontology. St. Louis.
Journal of Hygiene. London.
Journal of Immunology. Baltimore.
Journal of the Indiana State Medical Association. Indianapolis.
Journal of Infectious Diseases. Chicago.
Journal of International College of Surgeons. Chicago.
Journal of Investigative Dermatology. Baltimore.
Journal of the Iowa State Medical Society. Des Moines.
Journal of the Kansas Medical Society. Topeka.
Journal of the Kentucky State Medical Association. Bowling Green.
Journal of Laboratory and Clinical Medicine. St. Louis.
Journal of Laryngology and Otology. London.

* Cannot be lent.

Journal of the Maine Medical Association. Portland.
Journal of the Medical Association of the State of Alabama. Montgomery.
Journal of the Medical Association of Georgia. Atlanta.
Journal of the Medical Society of New Jersey. Trenton.
Journal de médicine de Lyon. Lyon.
Journal of Mental Science. London.
Journal of the Michigan State Medical Society. Lansing.
Journal of the Missouri State Medical Association. St. Louis.
Journal of Mount Sinai Hospital. New York.
Journal of National Cancer Institute. Washington, D. C.
Journal of National Malaria Society. Columbia, S. C.
Journal of Nervous and Mental Disease. New York.
Journal of Neurology, Neurosurgery and Psychiatry. London.
Jouranl of Neuropathology and Clinical Neurology. Chicago.
Journal of Neuropathology and Experimental Neurology. Baltimore.
Journal of Neurophysiology. Springfield, Ill.
Journal of Neurosurgery. Springfield, Ill.
Journal of Nutrition. Philadelphia.
Journal of the Oklahoma State Medical Association. Oklahoma City.
Journal of Pathology and Bacteriology. Edinburgh.
Journal of Pediatrics. St. Louis.
Journal of Pharmacology and Experimental Therapeutics. Baltimore.
Journal of the Philippine Medical Association. Manila.
Journal of Physiology. London.
Journal of the South Carolina Medical Association. Florence.
Journal of the Student American Medical Association. Chicago.
Journal of the Tennessee State Medical Association. Nashville.
Journal of Thoracic Surgery. St. Louis.
Journal of Tropical Medicine and Hygiene. London.
Journal of Urology. Baltimore.
Journal of Venereal Disease Information. Washington, D. C.
Journal-Lancet. Minneapolis.
Klinische Wochenschrift. Berlin-Heidelberg.
Lancet. London.
Laryngoscope. St. Louis.
Maandschrift voor kindergeneeskunde. Leyden.
Medical Annals of the District of Columbia. Washington.
Medical Journal of Australia. Sydney.
Medicina. Buenos Aires.
Medicina. Mexico, D. F.
Medicina clínica. Barcelona.
Medicine. Baltimore.
Mental Hygiene. Albany, N. Y.
Metabolism. New York.
Military Surgeon. Washington, D. C.
Minerva medica. Turin.
Minerva pediatrica. Turin.
Minnesota Medicine. St. Paul.
Nebraska State Medical Journal. Lincoln.
Nederlandsch tijdschrift voor geneeskunde. Amsterdam.
Neurology. Minneapolis.
New England Journal of Medicine. Boston.
New Orleans Medical and Surgical Journal. New Orleans.
New York State Journal of Medicine. New York.
New Zealand Medical Journal. Wellington.
Nordisk medicin. Stockholm.
North Carolina Medical Journal. Winston-Salem.
Northwest Medicine. Seattle.
Ohio State Medical Journal. Columbus.
Pediatrics. Springfield, Ill.
Pennsylvania Medical Journal. Harrisburg.
Physiological Reviews. Baltimore.
Plastic & Reconstructive Surgery. Baltimore.
Policlinico (Med. Sect.). Rome.
Policlinico (Pract. Sect). Rome.
Postgraduate Medicine. Minneapolis.
Practitioner. London.
Prensa médica argentina. Buenos Aires.
Presse médicale. Paris.
Proceedings of Royal Society of Medicine. London.
Proceedings of the Society for Experimental Biology and Medicine. Utica, N. Y.
Proceedings of Staff Meetings of Mayo Clinic. Rochester, Minn.
Progrès médical. Paris.
Psychiatric Quarterly. Utica, N. Y.
Psychiatry. Washington, D. C.
Psychoanalytic Quarterly. Albany, N. Y.
Psychoanalytic Review. Albany, N. Y.
Psychosomatic Medicine. New York.
Public Health Reports. Washington, D. C.
Quarterly Journal of Medicine. Oxford.
Quarterly Journal of Studies on Alcohol. New Haven, Conn.
Radiology. Syracuse, N. Y.
Review of Gastroenterology. New York.
Revista de la Asociación médica argentina. Buenos Aires.
Revista brasileira de cirurgia. Rio de Janeiro.
Revista brasileira de gastroenterologia. Rio de Janeiro.
Revista clínica española. Madrid.
Revista clínica de São Paulo. São Paulo.
Revista médica de Chile. Santiago.
Revista médica de Costa Rica. San José.
Revista de medicina e cirurgia de São Paulo. São Paulo.
Revista de urología. México.
Revue médicale de Liège. Liège.
Revue du rhumatisme et des maladies osteo-articulaires. Paris.
Revue de la tuberculose. Paris.
Rhode Island Medical Journal. Providence.
Riforma medica. Naples.
Rivista di patologia e clinica della tubercolosi. Bologna.
Rocky Mountain Medical Journal. Denver.
Sang. Paris.
Scalpel. Brussels.
Schweizerische medizinische Wochenschrift. Basel.
Schweizerische Zeitschrift für Tuberkulose. Basel.
Science. Washington, D. C.
Semaine des hôpitaux de Paris. Paris.
Settimana medica. Florence.
South African Medical Journal. Cape Town.
South Dakota Journal of Medicine and Pharmacy. Sioux Falls
Southern Medical Journal. Birmingham, Ala.
Southwestern Medicine. El Paso, Texas.
Stanford Medical Bulletin. San Francisco.
Strahlentherapie. Munich.
Surgery. St. Louis.
Surgery, Gynecology and Obstetrics. Chicago.
Texas State Journal of Medicine. Fort Worth.
Thorax. London.
Tidsskrift for den norske lægeforening. Oslo.
Tubercle. London.
Ugeskrift for læger. Copenhagen.
United States Armed Forces Medical Journal. Washington, D. C.
Urologic and Cutaneous Review. West Palm Beach, Fla.
Virginia Medical Monthly. Richmond.
Western Journal of Surgery, Obstetrics and Gynecology. Portland, Ore.
West Virginia Medical Journal. Charleston.
Wiener klinische Wochenschrift. Vienna.
Wiener medizinische Wochenschrift. Vienna.
Wisconsin Medical Journal. Madison.
World Medical Association Bulletin. New York.
Yale Journal of Biology and Medicine. New Haven.
Zeitschrift für Geburtshilfe und Gynäkologie. Stuttgart.
Zeitschrift für die gesamte experimentelle Medizin. Heidelberg.
Zeitschrift für Kinderheilkunde. Heidelberg.
Zeitschrift für klinische Medizin. Heidelberg.
Zentralblatt für Chirurgie. Leipzig.
Zentralblatt für Gynäkologie. Leipzig.

SUBJECT INDEX

This is an index to all the reading matter in THE JOURNAL. In the Current Medical Literature Department only the articles which have been abstracted are indexed.

The letters used to explain in which department the matter indexed appears are as follows: "BI," Bureau of Investigation; "E," Editorial; "C," Correspondence; "ab," abstracts; the asterisk (*) indicates an original article in THE JOURNAL.

This is a subject index and one should, therefore, look for the subject word, with the following exceptions: "Book Notices," "Deaths," "Medicolegal Abstracts" and "Societies" are indexed under these titles at the end of the letters "B," "D," "M," and "S." Matter pertaining to the Association is indexed under "American Medical Association." The name of the author, in brackets, follows the subject entry.

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Acad.—Academy *Indust.—Industrial*
Am.—American *Inst.—Institute*
A.—Association *Internat.—International*
Coll.—College *M.—Medical*
Commn.—Commission *Med.—Medicine*
Comm.—Committee *Nat.—National*
Conf.—Conference *Pharm.—Pharmaceutical*
Cong.—Congress *Phys.—Physicians*
Dist.—District *Soc.—Society*
Div.—Division *Surg.—Surgery*
Found.—Foundation *Surgs.—Surgeons*
Hosp.—Hospital *S.—Surgical*

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*Bronstein, M. R., and Witkind, E.: Am. J. Med. Sci. *222*, 677, Dec., 1951.

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